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TRANSACTIONS

OF THE

ASSOCIATION OF AMERICAN PHYSICIANS.

FOURTEENTH SESSION,

HELD AT WASHINGTON, D. C.,

MAY 2, 3, AND 4, 1899.

VOLUME XIV.

PHILADELPHIA:
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ASSOCIATION OF AMERICAN PHYSICIANS

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ALTERNATE REPRESENTATIVE.

C. F. FOLSOM, M.D.

OFFICERS OF THE ASSOCIATION.

(FROM ITS ORGANIZATION TO THE PRESENT TIME.

Year.	*President.*	*Vice-President.*	*Recorder.*	*Secretary.*	*Treasurer.*
1886.	Francis Delafield.	....	.....	James Tyson.	A. B. Ball.
1887.	S. Weir Mitchell.	Francis Minot. R. Palmer Howard.	J. T. Whittaker.	Geo. L. Peabody.	W. W. Johnston.
1888.	Wm. H. Draper.	Francis Minot. R. Palmer Howard.	William Osler.	Henry Hun.	W. W. Johnston.
1889.	Francis Minot.	R. Palmer Howard. S. C. Busey.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1890.	S. C. Busey.	William Pepper. Henry M. Lyman.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1891.	Wm. Pepper.	Henry M. Lyman.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1892.	Henry M. Lyman.	George Ross.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1893.	A. L. Loomis.	Reginald H. Fitz.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1894.	Reginald H. Fitz.	William Osler.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1895.	Wm. Osler.	A. Jacobi.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1896.	A. Jacobi.	J. M. Da Costa.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1897.	J. M. Da Costa.	F. C. Shattuck.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1898.	F. C. Shattuck.	G. Baumgarten.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1899.	G. Baumgarten.	E. G. Janeway.	I. Minis Hays.	Henry Hun.	W. W. Johnston.
1900.	E. G. Janeway.	Wm. H. Welch.	I. Minis Hays.	Henry Hun.	J. P. C. Griffith.

MEMBERS.

* Original Members.

ELECTED

1892. ABBOTT, ALEXANDER C., M.D., Laboratory of Hygiene, University of Pennsylvania, Philadelphia.
1896. ABEL, JOHN J., M.D., 1604 Bolton St, Baltimore.
1894. ADAMI, J. GEORGE, M.D., Pathological Laboratory, McGill University, Montreal, Canada.
*1886. ADAMS, J. F. A., M.D., 26 Wendell Ave., Pittsfield, Mass.
1896. ADLER, ISAAC, M.D., 12 E. 60th St., New York.
*1886. ATKINSON, I. E., M.D., 605 Cathedral St., Baltimore.
*1886. BALL, A. BRAYTON, M.D., 42 W. 36th St., New York.
1899. BARKER, L. F., M.D., Johns Hopkins Hospital, Baltimore.
*1886. BAUMGARTEN, G., M.D., 2643 Chestnut St, St. Louis.
1894. BIGGS, HERMAN M., M.D., 5 W. 58th St., New York.
1895. BILLINGS, FRANK, M.D., 235 State St., Chicago.
1898. BLACKADER, A. D., M.D., 236 Mountain St., Montreal, Canada.
1892. BOLTON, B. MEADE., M.D., 294 Nassau St., Princeton, N. J.
1890. BOND, CHARLES S., M.D., 112 N. 10th St., Richmond, Ind.
1898. BRANNAN, JOHN W., M.D., 11 W. 12th St., New York.
1888. BRIDGE, NORMAN, M.D., 217 S. Broadway, Los Angeles, Cal.
*1886. BUSEY, SAMUEL C., M.D., 1545 I St. (N. W.), Washington, D. C.
1899. CABOT, R. C., M.D., 190 Marlborough St., Boston, Mass.
1889. CARY, CHARLES, M.D., 340 Delaware Ave., Buffalo, N. Y.
1898. COHEN, S. SOLIS, M.D., 219 S. 17th St., Philadelphia.
*1886. COUNCILMAN, WILLIAM T., M.D., Harvard Medical School, Boston.
1897. CUSHNY, ARTHUR R., M.D., University of Michigan, Ann Arbor, Mich.
1894. CUTLER, ELBRIDGE G., M.D., 214 Beacon St., Boston.
*1886. DA COSTA, J. M., M.D., 1700 Walnut St., Philadelphia.
1888. DANA, CHARLES L., M.D., 50 W. 46th St., New York.
1888. DANFORTH, I. N., M D., 758 W. Adams St., Chicago.

ELECTED

*1886. DELAFIELD, FRANCIS, M.D., 12 W. 32d St., New York.
1893. DOCK, GEORGE, M.D., 14 Cornwell Place, Ann Arbor, Mich.
*1886. DRAPER, WILLIAM H., M.D., 19 E. 47th St., New York.
*1886. EDES, ROBERT T., M.D., 58 Eliot St., Jamaica Plain, Mass.
1899. ELY, JOHN S. M.D., 60 Wall St., New Haven, Conn.
1888. ERNST, HAROLD C., M.D., 8 Greenough Ave., Jamaica Plain, Mass.
1890. FISK, SAMUEL A., M.D., 37 18th Ave., Denver, Col.
*1886. FITZ, REGINALD H., M.D., 18 Arlington St., Boston.
1895. FISCHEL, W. E., M.D., 2647 Washington Ave., St. Louis.
1895. FLEXNER, SIMON, M.D., Johns Hopkins Hospital, Baltimore.
*1886. FOLSOM, CHARLES F., M.D., 15 Marlborough St., Boston.
*1886. FORCHHEIMER, F., M.D., 160 W. 9th St., Cincinnati.
1894. FUSSELL, M. HOWARD, M.D., 189 Green Lane, Manayunk, Philadelphia.
*1886. GRAHAM, J. E., M.D., 134 Bloor St., E. Toronto, Canada.
1890. GRIFFITH, J. P. CROZER, M.D., 123 S. 18th S., Philadelphia.
*1886. GUITÉRAS, JOHN, M.D., 130 S. 39th St., Philadelphia.
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*1886. HAYS, I. MINIS, M.D., 266 S. 21st St., Philadelphia.
1897. HEKTOEN, LUDVIG, M.D., Rush Medical College, Chicago.
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1898. HERRICK, JAMES B., M.D., 751 Warren Ave., Chicago.
1898. HERTER, C. A., M.D., 819 Madison Ave., New York.
*1886. HUN, HENRY, M.D., 149 Washington Ave., Albany.
1890. HURD, HENRY MILLS, M.D., Johns Hopkins Hospital, Baltimore.
*1886. JACOBI, A., M.D., 110 W. 34th St., New York.
1899. JAMES, WALTER B., M.D., 17 W. 54th St., New York.
*1886. JANEWAY, E. G., M.D., 36 W. 40th St., New York.
1899. JOHNSTON, W. G., M.D., 74 Shuter St., Montreal, Canada.
*1886. JOHNSTON, W. W., M.D., 1603 K St. (N. W.), Washington, D. C.
*1886. KINNICUTT, FRANCIS P., M.D., 42 W. 37th St., New York.
1895. LAFLEUR, HENRI A., M.D., 58 University St., Montreal, Canada.
1890. LATIMER THOMAS S., M.D., 211 Monument St., Baltimore.
1888. LEWIS, MORRIS J., M.D., 1316 Locust St., Philadelphia.
*1886. LONGSTRETH, MORRIS, M.D., 1416 Spruce St., Philadelphia.
1889. LOVING, STARLING, M.D., 229 E. State St., Columbus, Ohio.
*1886. LYMAN, HENRY M., M.D., 220 Ashland Boulevard, Chicago.

ELECTED

1891. McPhedran, A., M.D., 84 College St., Toronto, Canada.
1898. Mallory, F. B., M.D., Department of Pathology, Harvard Medical School, Boston.
1891. Mason, A. Lawrence, M.D., 265 Clarendon St., Boston.
1887. Meigs, Arthur V., M.D., 1322 Walnut St., Philadelphia.
1892. Meltzer, S. J., M D., 66 E. 124th St., New York.
1898. Mitchell, John K., M.D., 256 S. 15th St., Philadelphia.
*1886. Mitchell, S. Weir, M.D., 1524 Walnut St., Philadelphia.
1887. Musser, John H., M.D., 1927 Chestnut St., Philadelphia.
1891. Northrup., W. P., M.D., 57 E. 79th St., New York.
*1886. Osler, William, M.D., 1 W. Franklin St., Baltimore.
1898. Packard, Frederick A., M.D., 110 S. 18th St., Philadelphia.
1899. Park, William H., M.D., 315 W. 76th St. New York.
*1886. Peabody, George L., M.D., 57 W. 38th St., New York.
1898. Pfaff, Franz, M.D., 871 Boylston St., Boston.
1888. Prentiss, D. W., M.D., 1011 14th St. (N. W.), Washington, D C.
1899. Prince, Morton, M.D., 458 Beacon St., Boston.
*1886. Prudden, T. Mitchell, M.D., 160 W. 59th St., New York.
*1886. Putnam, James J., M.D., 106 Marlborough St., Boston.
1894. Rachford, B. K., M.D., 117 Broadway, Cincinnati.
1896. Reed, Walter, M.D., Army Medical Museum and Library, Washington, D. C.
*1886. Robinson, Beverley, M.D., 37 W. 35th St., New York.
1893. Rotch, T. M., M.D., 197 Commonwealth Ave., Boston.
1898. Sachs, B., M.D., 21 E. 65th St., New York.
*1886. Shattuck, Frederick C., M.D., 135 Marlborough St., Boston.
*1886. Shattuck, George B., M.D., 183 Beacon St., Boston.
*1886. Sinkler, Wharton, M.D., 1606 Walnut St., Philadelphia.
*1886. Smith, A. A., M.D., 40 W. 47th St., New York.
1891. Smith, Andrew H, M.D., 18 E. 46th St., New York.
1892. Smith, Theobald, M.D., South Street, Forest Hills, Boston.
1887. Starr, Louis, M.D., 1818 S. Rittenhouse Square, Philada.
1887. Starr, M. Allen, M.D., 5 W. 54th St., New York.
1898. Stengel, Alfred, M.D., 332 S. 17th St., Philadelphia.
*1886. Sternberg, George M., M.D., U.S.A., Surgeon-General's Office. Washington, D. C.
1896. Stewart, D. D., M.D., 108 S. 17th St., Philadelphia.
*1886. Stewart, James, M.D., 285 Mountain St., Montreal, Canada.
1889. Stockton, Charles G, M.D., 436 Franklin St., Buffalo New York.

ELECTED

1899. THACHER, J. S., M.D., 33 W. 39th St., New York.
1897. THAYER, W. S., M.D., Johns Hopkins Hospital, Baltimore.
1889. THOMPSON, W. GILMAN, M.D., 34 E. 31st St., New York.
1889. THOMSON, WILLIAM H., M.D., 7 W. 56th St., New York.
*1886. TRUDEAU, EDWARD L., M.D., Saranac Lake, Franklin Co., New York.
*1886. TYSON, JAMES, M.D., 1506 Spruce St., Philadelphia.
1895. VAN GIESEN, IRA T., M.D., 1 Madison Ave., New York.
1889. VAUGHAN, VICTOR C., M.D., University of Michigan, Ann Arbor, Michigan.
1898. VICKERY, HERMAN F., M.D., 263 Beacon St., Boston.
1889. WALCOTT, HENRY P., M.D., 11 Waterhouse St., Cambridge, Mass.
*1886. WARD, SAMUEL B., M.D., 281 State St., Albany, N. Y.
*1886. WELCH, WILLIAM H., M.D., 935 St. Paul St., Baltimore.
1898. WESBROOK, F. F., M.D., State Board of Health, Minneapolis.
*1886. WHITTAKER, JAMES T., M.D., 32 Garfield Place, Cincinnati.
*1886. WILKINS, GEORGE, M.D., 899 Dorchester St., Montreal, Canada.
1894. WILLIAMS, FRANCIS H., M.D., 505 Beacon St , Boston.
*1886. WILSON, JAMES C., M.D., 1437 Walnut St., Philadelphia.
1898. WITHINGTON, CHARLES F., M.D., 1 Elm Hill Ave., Roxbury, Mass.
*1886. WOOD, HORATIO, M.D., 1925 Chestnut St., Philadelphia.
1899. WRIGHT, J. H., M.D., Pathological Laboratory, Massachusetts General Hospital, Boston, Mass.

HONORARY MEMBERS.

Elected Active Member.	Elected Honorary Member.	
1886.	1887.	BILLINGS, JOHN S., M.D., Astor Library, Lafayette Place, New York.
1886.	1897.	CHEW, SAMUEL C., M.D., 215 W. Lanvale St., Baltimore.
.	1886.	CLYMER, MEREDITH, M.D., 65 W. 38th St., New York.
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1886.	1898.	POLK, WM. M., M.D., 7 E. 36th St., New York.
	1886.	STILLÉ, ALFRED, M.D., 3900 Spruce St., Philadelphia.

DECEASED MEMBERS.

Date of Election.	
*1890.	BARKER, FORDYCE, M.D., New York.
*1886.	BOWDITCH, HENRY I., M.D., Boston.
1886.	BRUEN, EDWARD T., M.D., Philadelphia.
*1886.	CLARK, ALONZO, M.D., New York.
1889.	DABNEY, WILLIAM C., M.D., University of Virginia.
*1886.	DALTON, JOHN C., M.D., New York.
1886.	DONALDSON, FRANK, M.D., Baltimore.
1886.	FORMAD, HENRY F., M.D., Philadelphia.
1889.	GEDDINGS, W. H., M.D., Aiken, S. C.
1886.	HOWARD, R. PALMER, M.D., Montreal, Canada.
1886.	HUDSON, E. DARWIN, JR., M.D., New York.
1886.	HUTCHINSON, JAMES H., M.D., Philadelphia.
1886.	JOHNSON, HOSMER A., M.D., Chicago.
*1886.	LEIDY, JOSEPH, M.D., Philadelphia.
1886.	LOOMIS, ALFRED L., M.D., New York.
1886.	MCBRIDE, THOMAS A., M.D., New York.
1890.	MACDONNELL, R. L., M.D., Montreal, Canada.
1886.	PEPPER, WILLIAM, M.D., Philadelphia.
1887.	REEVES, JAMES E., M.D., Chattanooga, Tenn.
*1886.	ROCHESTER, THOMAS F., M.D., Buffalo, N. Y.
1889.	ROOSEVELT, J. WEST, M.D., New York.
1886.	ROSS, GEORGE, M.D., Montreal, Canada.
1886.	SCHMIDT, H. D., M.D., New Orleans.
1886.	THACHER, JAMES K., M.D., New Haven, Conn.

* Honorary Members.

ASSOCIATION

OF

AMERICAN PHYSICIANS.

CONSTITUTION

AS AMENDED MAY 2, 1899.

ARTICLE I.

Object and Name.

This Association has for its object the advancement of scientific and practical medicine, and shall be known as THE ASSOCIATION OF AMERICAN PHYSICIANS.

ARTICLE II.

Members.

The number of active members shall be limited to one hundred and twenty-five. Physicians of sufficient eminence to merit the distinction may, to a number not exceeding twenty-five, be elected honorary members, and as such shall be entitled to attend all meetings and to take part in the proceedings, but not to vote.

Membership shall lapse by reason of absence from three successive annual meetings without reason given acceptable to the Council. An excused absence shall not be regarded as an attendance. Membership may be forfeited for reasons deemed sufficient by the Association.

ARTICLE III.

Officers.

The Officers of the Association shall be a President, a Vice-President, a Secretary, a Recorder, a Treasurer—all to be elected annually;

five Councillors—one to be elected each year for a term of five years; and a Representative to serve on the Executive Committee of the Congress of American Physicians and Surgeons, to be elected at the annual meeting immediately following the Congress.

Article IV.

Duty of Officers.

The duties of the President, Vice-President, Secretary, and Treasurer shall be those usually assigned to these officers.

The Recorder shall secure the papers read and also proper notes of the discussions thereon, and shall publish the annual volume of TRANSACTIONS.

The five Councillors shall constitute a Committee of Nomination of Officers, and as such shall present a report at the commencement of the morning session of the last day of the annual meeting, at the conclusion of which session the election shall be held by ballot.

The Representative on the Executive Committee of the Congress shall have full power to represent the Association on all ordinary questions, but must be authorized by the Council of this Association before assenting to the admission of any Society to the Congress.

Article V.

Council.

The officers of the Association shall constitute the Council, of which four members shall constitute a quorum. It shall be the duty of the Council to supervise the affairs of the Association, to make all the arrangements for the annual meeting, to suggest the subject for debate, and to consider the nominations for membership and report on them at the meeting at which they shall be balloted on.

Article VI.

Meetings.

1. The Association shall hold an annual meeting in the City of Washington, D. C., at a time designated by the Council.

2. The President shall call the meeting to order and open the session by an address not exceeding half an hour in length. In his absence the Vice-President shall preside, and in the absence of both these officers, the senior Councillor.

3. Then shall follow original communications, discussions on subjects of general interest in the department of medicine and pathology, demonstrations in pathology, and miscellaneous business.

4. Authors of papers, and referees and co-referees who open a discussion shall not occupy more than thirty minutes each; and in the discussion following, the remarks of each speaker shall be limited to ten minutes.

5. The referees, co-referees, and authors of papers shall send abstracts of their papers to the Council for distribution to members previous to the meeting.

Article VII.

Quorum.

Any number of members present at the appointed time of the annual meeting shall constitute a quorum for the transaction of ordinary business, but for the election of members, fifteen shall be necessary for a quorum; and for altering the Constitution, twenty-five members shall be necessary.

Article VIII.

Election of Members.

Nominations to membership, signed by two members who are not officers of the Association, must be made in writing at an annual meeting of the Association; and within six months of the time of nomination the nominators shall transmit to the Council letters stating the qualifications of the nominee, and also a list of his professional positions and publications. The Council shall report the name of each nominee to the members of the Association by letter prior to acting upon the same. The Council shall report those nominations which are approved by it to the next annual meeting for action. The election of new members shall take place on the second day of the meeting. An affirmative vote of three-fourths of the members present shall be necessary for the election of active members, but for the election of honorary members a unanimous vote of those present shall be required.

Article IX.

Annual Dues.

The annual dues of the Association shall be such sum as the Council from time to time may fix, from the payment of which honorary members shall be exempt.

Article X.

Amendments to the Constitution.

Amendments to the Constitution must be proposed in writing by five members at an annual meeting and must be acted upon at the succeeding annual meeting, the notices for which shall contain an announcement of the proposed amendments; and such amendments shall require for their adoption an affirmative vote of three-fourths of those present.

MINUTES

OF THE

FOURTEENTH ANNUAL MEETING,

Held in Washington, D. C., May 2, 3, *and* 4, 1899.

THE following members were present during the meeting:

A. C. Abbott.	Henry Hun.	J. J. Putnam.
J. G. Adami.	Henry M. Hurd.	B. K. Rachford.
J. F. A. Adams.	A. Jacobi.	T. M. Rotch.
I. E. Atkinson.	E. G. Janeway.	B. Sachs.
G. Baumgarten.	W. W. Johnston.	Wharton Sinkler.
C. S. Bond.	F. P. Kinnicutt.	M. A. Starr.
S. C. Busey.	Henri A. Lafleur.	A. Stengel.
Charles Cary.	M. Longstreth.	G. M. Sternberg.
S. Solis Cohen.	H. M. Lyman.	D. D. Stewart.
A. R. Cushny.	Arthur V. Meigs.	J. Stewart.
I. N. Danforth.	S. J. Meltzer.	C. G. Stockton.
George Dock.	J. K. Mitchell.	W. H. Thomson.
S. A. Fisk.	J. H. Musser.	E. L. Trudeau.
R. H. Fitz.	W. P. Northrup.	James Tyson.
C. F. Folsom.	William Osler.	V. C. Vaughan.
F. Forchheimer.	F. A. Packard.	S. B. Ward.
J. P. C. Griffith.	C. L. Peabody.	W. H. Welch.
I. Minis Hays.	Franz Pfaff.	G. Wilkins.
F. P. Henry.	D. W. Prentiss.	J. C. Wilson.
J. B. Herrick.	T. M. Prudden.	W. S. Thayer.
C. A. Herter.		

TUESDAY, MAY 2D—MORNING SESSION.

The Association was called to order at 10.15 A.M. by President Baumgarten, who delivered the following introductory remarks:

In opening this fourteenth session, my first impulse is to express to you my respect by the briefness of my opening words, and to record my

appreciation of the high honor you have conferred upon me. In the face of my clear recognition that the greatness of the position in which I find myself is not mine by right of birth nor by achievement, I can only excuse my acceptance of it by my literal faith in the words of your first President, when he spoke of this Association as one in which no one will care who are the officers and who are not, and by the loyal interest I have ever taken and shown in its welfare.

This Association was founded as one of a number of special societies cultivating special branches of medicine; and for a specialty, too, which came near being forgotten in the recent splitting up of the domain of medicine into what began to look very much like fragments. In this sense the Association stands for specialization, for subdivision of labor, for concentration of effort on the part of the investigator and clinical observer. Nevertheless, it differs from our allied sister societies in some essential respects. From its very inception it counteracted some of the disadvantages of specialization by allying the clinician with the pathologist, the bacteriologist, and the chemist; it prevented one-sided devotion to the merely technical training of the practitioner in one department of medicine by providing for the cultivation of the disciplines upon which that training must be based—not only for the practice of internal medicine, but of all the other specialties of the healing art. More distinctly than in the other societies, a part of our discussions has been devoted to the scientific basis upon which all medical doctrines rest. Thus we can hope to preserve a just balance in the conflict of the opposing elemental tendencies—that of generalization, which in its extreme flights may lead to empty dogmatism, and that of specialization, which, uncontrolled, will run into routine.

Indeed, the increasingly valuable series of volumes of our TRANSACTIONS reflect clearly both these movements in the work of the Association—that of delving for scientific detail as well as its converse, the search for common stand-points, the desire to find the interdependence of morbid processes, to discover underlying general causes and common origins. We count among our members those who direct their labor and acumen to the quest of the most intricate details, as well as the master minds who, trained to the appreciation of the smallest factors, yet survey all that upon which the light of science shines from vantage ground.

Since last we met we have lost one of our master workers. It is incumbent on me to make the formal announcement of the death of Dr. William Pepper. A eulogy in this presence is supererogatory. This body, which owes so much of its early success to the tactful organizing efforts of Dr. Pepper, mingles its sorrow with that of the profession of all America,

that of the University of Pennsylvania, that of his native city. He was not only one of the founders but one of the able organizers, to whom this Association owes its existence; and we remember with gratitude the kindly influence of his presence among us—one of the most interested of our members, readiest in discussion, lavish of instruction, always competent and willing to give more than he received. May the Association long be spared another such loss!

The Treasurer read his annual report, which was referred to an Auditing Committee consisting of Drs. Janeway and Folsom.

The following amendment to the Constitution was unanimously adopted by the twenty-eight members present: "That in Art. VIII. of the Constitution, immediately before the last sentence, shall be inserted the words: 'The election of new members shall take place on the second day of the meeting.'"

It was recommended to the Council, that except in Congress years the Association limits its meeting to two days, and that on the first day the session should commence at 11 o'clock.

Dr. J. P. Crozer Griffith read a paper entitled "Congenital Idiopathic Dilatation of the Colon."

Dr. R. H. Fitz read a paper entitled "The Relation of Idiopathic Dilatation of the Colon to Phantom Tumor." These two papers were discussed by Drs. Osler, Jacobi, Griffith, and Fitz.

Dr. Tyson read a paper entitled "A Case of Presystolic Mitral Murmur Associated with Systolic Tricuspid Murmur Complicating Pregnancy," which was discussed by Drs. Janeway, Cary, Griffith, and Tyson.

Dr. Henry read a paper entitled "A Case of Mitral Stenosis, with Fever (now Malarial) of a Relapsing Type," which was discussed by Drs. Dock, Johnston, Cary, Thomson, Bond, and Henry.

Dr. Stengel read a paper entitled "The Immediate and Remote Effects of Athletics upon the Heart," which was discussed by Drs. Jacobi, Meigs, Folsom, Osler, Putnam, Dock, and Stengel.

The Auditing Committee reported that they had examined the Treasurer's report and vouchers and found them to be correct.

Adjourned at 12.45 P. M.

Afternoon Session.

The Association was called to order by President Baumgarten at 2.45 P.M.

Dr. Cushny read a paper entitled "On the Interpretation of Pulse-tracings," which was discussed by Drs. Dock, Jacobi, and Cushny.

Dr. Putnam read, in behalf of himself and Dr. Warren, a paper entitled "On the Operative Treatment of Spinal Tumors," which was not discussed.

Dr. Starr read a paper on "Tabes," which was discussed by Drs. Putnam, Sinkler, Thomson, Folsom, Bond, Sachs, Cary, Janeway, and Starr.

Dr. Herrick read a paper on "Kernig's Sign in Meningitis," which was discussed by Drs. Osler and Griffith.

Dr. Wilson read a paper on "Astasia-abasia, with a Case," which was discussed by Drs. Thomson, Henry, and Wilson.

Dr. J. K. Mitchell read a paper entitled "A Case of Family Periodic Paralysis," which was discussed by Dr. Putnam.

The Association adjourned at 5.15 P.M.

Wednesday, May 3d—Morning Session.

The Association was called to order at 10.15 A.M.

The following nominees, recommended by the Council, were elected members of the Association:

Drs. J. B. Thacher, W. B. James, and Wm. H. Park, of New York; Drs. R. C. Cabot, M. Prince, and J. H. Wright, of Boston; Dr. John S. Ely, of New Haven; Dr. L. F. Barker, of Baltimore; Dr. W. G. Johnston, of Montreal.

Dr. Israel T. Dana, of Portland, Maine, was elected an Honorary Member.

Dr. W. W. Johnston read a paper entitled "The Continued Fever of Epidemic Influenza," which was not discussed.

Dr. Vaughan read a paper entitled "Some Remarks on Typhoid Fever among our American Soldiers in the Recent War with Spain," which was discussed by Drs. Sternberg, Kinnicutt, Peabody, Dock, Jacobi, Prentiss, Cohen, and Vaughan.

Dr. Welch made a report of "A Case of Hæmochromatosis," which was discussed by Drs. Osler (who exhibited to the Association an analogous case), Adami, and Welch.

Dr. Musser read a paper entitled "Further Notes on a Case of Malta Fever."

The Association adjourned at 1 P.M.

Afternoon Session.

The Association was called to order by President Baumgarten at 2.35 P.M.

Dr. Meltzer read a paper entitled "Remarks on Otitis Media and

Earache in Lobar Pneumonia of Children," which was discussed by Drs. Jacobi, Kinnicutt, Rotch, and Meltzer.

Dr. Packard read a paper entitled "Endocarditis of Tonsillar Origin, with a Report of Five Cases," which was discussed by Drs. Tyson, Thayer, Thomson, Dock, Meltzer, and Packard.

Dr. Dock read a paper entitled "A Fatal Case of Epistaxis, with a Study of the Blood," which was discussed by Drs. Thayer, Stengel, and Osler.

Dr. Adami, in behalf of himself, Maud E. Abbott, and F. J. Nicholson, read a paper entitled "On the Diplococcus Form of the Colon Bacillus," which was discussed by Drs. Welch and Adami.

Dr. James Stewart read a paper entitled "Tumors Involving the Hypophysis," which was discussed by Dr. Starr.

Dr. Thayer demonstrated an "Acromegalic Skeleton," which was discussed by Drs. Osler and Putnam.

The Association adjourned at 6 P.M.

THURSDAY, MAY 4TH—MORNING SESSION.

The Association was called to order at 10.10 A.M. by President Baumgarten.

The Secretary read the nominations for officers of the Association for the ensuing year recommended by the Councillors.

Dr. Pfaff, on behalf of himself and Dr. Putnam, read a paper entitled "An Experimental Research Indicating that Paraxanthin-poisoning is not the Cause of Epilepsy or Migraine," which was discussed by Drs. Rachford, Herter, and Pfaff.

Dr. Herter read a paper entitled "The Action of Hepatic, Renal, and other Cells upon Phenol and Indol under Normal and Pathological Conditions," which was not discussed.

Dr. Forchheimer, on behalf of himself and Dr. R. W. Stewart, read a paper entitled "On the Toxicity of the Urine," which was not discussed.

Dr. Rotch read a paper entitled "Perforation of the Stomach by a Foreign Body in an Infant Seven Weeks Old," which was not discussed.

Dr. Williams' paper, entitled "A Small Aneurism of the Descending Arch of the Aorta, X-ray Examination Confirmed by Autopsy," was read by the Secretary.

During the meeting the following papers were read by title:

"Peculiarities of Eruption in Typhoid Fever," by J. M. Da Costa.

"Types of Uric-acid Diathesis," by I. N. Danforth.

"Individualization in the Bath-treatment of Patients with Typhoid Fever," by S. Solis Cohen.

"The Organism of a Case of Blastomycetic Dermatitis," by L. Hektoen.

"The Application of Thyroid Extract in the Treatment of a Cerebral Neoplasm," by S. Loving.

The following ticket, recommended by the Councillors, was unanimously elected:

President—E. G. Janeway.
Vice-President—Wm. H. Welch.
Recorder—I. Minis Hays.
Secretary.—Henry Hun.
Treasurer—J. P. Crozer Griffith.
Councillor—Wm. T. Councilman.

It was resolved that the thanks and congratulations of the Association be extended to President Baumgarten for the success of the meeting.

It was resolved that the thanks of the Association be extended to Mr. Roessle for his courtesy in furnishing a room for the Association to hold its meetings in.

The Association adjourned at 12 M.

HENRY HUN,
Secretary.

PAPERS.

NOTICE.

THE Association assumes no responsibility for the statements and opinions expressed in the papers read at its meetings.

CONGENITAL IDIOPATHIC DILATATION OF THE COLON.

By J. P. CROZER GRIFFITH, M.D.,
OF PHILADELPHIA.

Dilatation of the colon may be produced by a variety of causes, and various subdivisions based on etiology have consequently been made by writers. The form most frequently seen is that occurring generally in adult life, the result of habitual constipation. In some instances obstinate fecal impaction has developed, followed by death. In certain cases the obstruction has been brought about by the constipation producing kinking of the bowel through the weight of the contained feces. In others there has developed narrowing of some part of the bowel through external pressure. In the case of a boy of five years, reported by Gee,[1] a cyst compressed the anus. Sometimes the constipation and dilatation appear to be the direct result of an acquired atony, itself depending upon a debilitated system, perhaps the result of some acute exhausting disease. This may occur even in children, as in a case of Gay's,[2] in which great sluggishness of the bowels, with abdominal distention, developed in a boy of seven years who had just recovered from typhus fever. All dilatations of the types mentioned may be properly designated "acquired."

In another class of cases dilatation is the result of some congenital stenosis or obstruction in the colon or rectum, which immediately or slowly causes distention to develop above it. Treves[3] reports such a case, and takes the ground that probably all cases of dilatation of the colon in young children are of this nature. But

[1] St. Bartholomew's Hospital Reports, 1884, xx. 20.
[2] Transactions of the Pathological Society of London, 1854, v. 174.
[3] Lancet, 1896, i. 276.

this view is not supported by the evidence of the numerous post-mortem examinations.

A third class of cases may be called congenital idiopathic dilatation of the colon, and to this class our present study is especially directed.

The term "idiopathic" is employed here, as often, in a necessarily broad and rather loose manner. I would use it to designate an innate tendency to dilatation which is not dependent upon discoverable organic cause. The form of dilatation to which the term applies is not due to stricture or occlusion of any kind. It is not caused by constipation, as in acquired cases, but is itself the cause of this symptom, since the presence of fecal impaction or of scybalous masses is not the rule in this disease. It is not the result of a shortened mesocolon or other discoverable organic condition producing kinking. Although the great length of the sigmoid flexure in infancy probably predisposes to the development of the dilatation, yet this is in itself not the cause in idiopathic cases, else we should find the disease much more frequent than it is. Besides, in nearly all cases it is not the sigmoid flexure alone which is distended. The dilatation is not due to paralysis and atony alone, since so many cases develop in apparently healthy children, and so many autopsies show, in fact, hypertrophy of the intestinal walls. It cannot be said, on the other hand, to be due to congenital over-development of the walls of the colon, causing rigidity, since not every case has shown sufficiently marked hypertrophy, and, in any event, there is no proof that the hypertophy is not a secondary development. It is not due to colitis, since statistics indicate that colitis is a terminal condition only. In fact, the term idiopathic expresses rather our state of ignorance, for there must naturally be some cause for the faulty tendency to dilatation in these cases. As to what this may be, however, we can do no more than theorize.

The term "congenital," too, requires comment, since it has been used by writers with different significations. I have employed it to designate not only an actual dilatation present at birth, but also the existence of a congenital tendency to early dilatation, the latter condition being probably much the more common. With this definition in mind we can understand how some cases—those of the severest type—suffered distention and constipation from earliest

infancy, as soon as food began to enter the colon, and they rapidly grew worse; others, with a less grade of the disease, resisted distention decidedly for a time or tolerated it well, although showing great lack of expulsive power always; and still others had periods of improvement in which the distention largely disappeared, although the faulty nature of the colon remained, and relapse occurred later in nearly every instance.

It is impossible, however, to draw a sharp and always applicable line of distinction between congenital idiopathic cases and those which are not so. In the absence of an autopsy we cannot affirm positively that no stenosis existed, even though we may have reason to believe it. So, too, in cases in which the early history is incomplete or unsatisfactory, it is impossible to be sure that the symptoms were present from birth or soon after. Again, in cases in which the symptoms were clearly somewhat late in appearing we cannot always conclude with certainty whether the constipation present was a cause or a result of the dilatation. Consequently the cases selected as illustrations of idiopathic dilatation of the colon, and on which classifications have been based, differ with writers, and are not always the same, according as the writers' conceptions of the definition of idiopathic and congenital differed. I have therefore studied the originals of all the published reports of cases as far as these are known to me, and, that those interested may judge for themselves, I have avoided the tabulation of symptoms or mere enumeration of cases, but have given abstract synopses of those cases which seemed to have any claim whatever to be regarded as congenital idiopathic dilatation of the colon. In a secondary list, not used here for purposes of study and analysis, I have mentioned briefly most of the other cases quoted in medical literature, but which, for reasons given with each, it would seem should be excluded from this category. It should be stated that although most of these cases have been called idiopathic, they are not commonly described as congenital.

Before giving the synopses I wish to relate the following history of a case once under my own observation:

Roy S., born June, 1894, and aged, at the time of examination, two years and eleven months. The family history was good. He had never been ill except for constipation, which he had more or less since birth, and for which

very strong purgatives were required. When he was five months old marked distention of the abdomen began, with more or less pain nearly all the time. The child would sometimes go as long as a week before a movement could be obtained, but would then have diarrhœa for several days, with even increased gaseous distention of the abdomen. This condition persisted with little change until November, 1896, except for about a couple of months of each of his two summers, at which times the bowels would move naturally. In November, 1896, being then about two years and five months old, he was supposed to have swallowed a campaign button, and all purgative medicine was stopped for a week, after which it seemed well-nigh impossible to procure an evacuation, and the child had such pain and was so swollen that the parents "feared he would burst." Relief was obtained, at least to a degree, by the use of a rectal tube, which allowed the gas to escape; but the necessity of using the tube often daily, and of giving purgatives and enemata, persisted, and finally the procedures ceased to give much relief. He was brought to the hospital of the University of Pennsylvania, May 21, 1897. The following notes are abstracted from the clinical history:

Condition on Admission. The patient is a well-nourished child, slightly pale, intelligent, and bright. The abdomen is enormously protruding, tympanic everywhere upon percussion, and measures 63.5 cm. (25 in.) at the umbilicus and 69.8 cm. (27½ in.) at the most prominent portion. (Plate 1.) The umbilicus is pouting, and active peristaltic movements can be seen. The outline of the greatly enlarged colon is at times distinctly visible. No tumor can be felt anywhere. There is a large amount of veining over the trunk. The costal margin is very much everted by the pressure of the gas in the bowels. Ordered hot fomentations to relieve pain, the insertion at times of a rectal tube, enemata of soap and water, followed by some containing turpentine and sometimes asafœtida. Milk diet was given.

May 22d. The child retained the enemata for some hours, and finally passed a large bowel movement, which reduced the size of the abdomen a trifle.

23d. Strychnine ordered internally.

June 7th. The child has continued in much the same condition, and there has been vomiting on two or three occasions. A daily enema of milk of asafœtida has been given, and the milk diet continued, with, later, a little beef-juice added. Hot fomentations have been employed frequently, also high, laxative enemata, which relieved the distention slightly. There is not much pain, and the child is bright, but homesick. Yesterday morning he developed slight, watery, greenish diarrhœa. About 5 P.M. he grew irritable and had silght pain; the temperature rose by evening to 105.2° F.; pulse 140, respiration 37. Local antipyretic measures were ordered, with whiskey, digitalis, and quinine. The diarrhœa continued, and last night there were ten stools. The abdomen is tense, and the child has some pain. The temperature is less this morning and the abdomen is smaller, but it still measures 58.4 cm. (23 in.) at the most prominent part. Paregoric ordered.

9th. Fever has persisted. The abdomen now measures 68.6 cm. (27 in.)

FIG. 1.

Case of Roy S.—Idiopathic Dilatation of the Colon.

FIG. 2.

Second Case—Probable Idiopathic Dilatation of the Colon.

at the umbilicus and 72.4 cm. (28½ in.) at the most prominent portion. The diarrhœa is gradually lessening, but the child refuses nourishment and is losing ground. Enemata and strychnine stopped and bismuth ordered.

11*th*. As the condition grew worse through failing strength and continued great abdominal distention, operation was advised. Right inguinal colotomy was done by Dr. John Ashhurst, Jr., the colon being opened shortly beyond the cæcum. A large amount of semi-liquid feces and of gas came away through the opening after an injection into it, and the abdomen became much more relaxed.

16*th*. During the rest of the eleventh and upon the following day a large amount of fecal matter was passed through the artificial anus, and the abdomen went down nearly to its natural size. The patient's general condition seemed at that time fairly good. The abdomen did not again become distended, but the child gradually failed in strength and died to-day.

The body was removed to the home of the parents and an autopsy performed there by Dr. R. J. Hillis, the physician who had sent the boy to the hospital. He reports that nothing was found abnormal in the belly except a marked constriction, about 25.4 cm. (10 in.) in length, situated in the ileum shortly above the cæcum. There was a small quantity of fecal matter above this. The ileum was not distended. There was no constriction found in the colon, and the abdomen was collapsed. No measurements of the colon were made, or any observation on the character of the intestinal walls.

I have seen a second case, which I believe to have been of the same nature as the one just described, although I do not include it as such, for want of a satisfactory clinical history.

The child suffered from habitual obstinate constipation, and had an enormously distended, tympanitic abdomen. It was seen a number of years ago in the medical clinic of the University of Pennsylvania, and was made the subject of a lecture by Dr. William Pepper. I had a photograph of it taken on the day of its single visit to the hospital. (Plate 2.) The presence of peritonitis was excluded, and the case was supposed to be one of extreme atony of the bowel. I now believe it to have been an idiopathic dilatation.

The following are the synopses of the cases which may with reason be considered congenital idiopathic dilatation of the colon. It will be noticed that the word "colon" has frequently been used by the writers to designate the large intestine, in contradistinction to the rectum and sigmoid flexure. In other instances it includes the sigmoid flexure as well as the rest of the colon. Each abstract shows what the writer has intended in this respect as far as he has made his meaning clear. The age given is in nearly every instance

that of the patient when first coming under continued observation. The "history" details the condition up to this time, while the result of the examination and of the continued observation is described after the words "under observation."

Henoch. (*Beiträge zur Kinderheilkunde*, 1861, 123.) *History.* Boy, aged one and three-quarter years. Great distention of abdomen, with constipation on the third day after birth. Condition continued, constipation sometimes lasting eight days; tympanites; purgatives of little use; enemata better; passage of syringe nozzle best, this bringing away large amounts of gas and feces, always soft, with considerable lessening of girth. *Under observation.* No obstruction discoverable in rectum. Under continued medication grew much better; daily stools; abdomen much smaller. But symptoms returned after treatment stopped. Child lost sight of.

Peacock. (*Transactions of the Pathological Society of London*, 1872, xxiii., 104.) *History.* Man, aged twenty-eight years. Constipated from birth; purgatives, and, later, enemata always required. Worse after a severe attack at seventeen years. Flatulence annoying and abdominal distention often great. Obstruction set in six weeks before death; relieved, but returned; belly enormous; flatus passed in large quantities; died unexpectedly. *Autopsy.* Large intestine from cæcum to upper rectum enormously distended, 15 to 20 cm. (6 to 8 in.) in diameter, containing semi-solid feces; ulceration of mucous membrane. Ileum somewhat distended; rectum healthy.

Gee (*St. Bartholomew's Hospital Reports*, 1884, xx. 19.) *Case I. History.* Boy, aged four and one-half years. At three months difficulty in defecation began, with hard stools. At twelve months swelling of abdomen began and constantly increased. *Under observation.* Great abdominal distention; coils of intestine visible; great dyspnœa; constipation, relieved by enemata; rectal tube brought away gas and gave some relief, the abdomen growing smaller. Lived a few weeks. Diarrhœa before death. *Autopsy.* Great elongation and enormous distention of sigmoid flexure; 10 cm. (4 in.) in greatest diameter; walls thickened. Sigmoid formed two huge sacs connected by a narrow strip of bowel. Rectum distended; colon natural.

Case II. History. Boy, aged four years. Great distention since one month old; habitual constipation. *Under observation.* Extreme tympanitic distention; hard feces felt in rectum. Died soon after. *Autopsy.* Distention of colon, especially of upper part of sigmoid flexure. Contraction of rectum and of lower part of sigmoid below a hard concretion. Semi-liquid feces above this; no real stenosis.

There appears no evidence that the concretion caused obstruction and dilatation, and this is apparently Gee's opinion also.

Bristowe. (*British Medical Journal*, 1885, i. 1086.) *History.* Girl, aged eight years. "Long been subject to constipation of the bowels." No stool for fully seven weeks; latterly constant vomiting. *Under observation.*

Distended abdomen, growing more so; no pain or tenderness; absolute constipation in spite of treatment; lived three weeks. *Autopsy.* Coils of distended intestine outlined through abdominal walls. After incision sigmoid flexure and descending and transverse colon found greatly distended, 7.6 to 9 cm. (3 to 3½ in.) in diameter. Ascending colon, cæcum, and small intestine also distended, but less so. Rectum distended to 5 cm. (2 in.) above anus. No stricture; thickening of muscular coat of large intestine; some ulceration of mucous membrane. Large intestine full of thick, semi-solid feces. Hardened mass above anus. No flatus.

Bristowe attributes the condition chiefly to the acute obstruction; yet the history of constipation for years, with the presence of marked hypertrophy of the walls of the colon, point strongly to a congenital origin.

Cheadle. (*Lancet*, 1886, ii. 1117.) *History.* Boy, aged three years. Tumidity of abdomen and obstinate constipation began at three months. All purgatives failed in turn; stools dry and hard; for two years almost never a stool without enema. Sometimes colon retained two or three enemata given in one day. *Under observation.* Abdomen greatly distended, especially in position of colon below ribs; girth 59 cm. (23¼ in.); tympanitic. Under treatment with mild laxatives and tonics improved, and recovery about complete, with daily stool, in two months.

Fütterer. (Virchow's *Archiv*, 1886, cvi. 555.) *History.* Boy, aged fourteen years. Abdomen distended from birth and grew larger slowly, but last year rapidly. Bowels moved about three times a day spontaneously. *Under observation.* Enormous abdomen, 91 cm. (35⅔ in.) in girth; tympanitic; no vomiting. Distention somewhat diminished by daily injection. Exploratory operation; nothing done; death. *Autopsy.* Sigmoid flexure distended into a huge sac; wall hypertrophied; no ulceration. Colon and rectum not distended. Passage from rectum into sac distorted, so that obstruction by pressure was produced.

Fütterer regards the case as an instance of true congenital malformation of the sigmoid flexure, which makes the propriety of including it in this list somewhat doubtful.

Hughes. (*Transactions of the Pathological Society of Philadelphia*, 1887, xiii. 40.) *History.* Boy, aged three years. Obstinate constipation in infancy; abdomen gradually grew larger and constipation worse; stools only after laxatives, but never hard. After entero-colitis at two years constipation more obstinate, and once lasted nineteen days. *Under observation.* Abdomen enormously enlarged; peristalsis of intestine visible; tympanites; no stool for twenty-four days. Improved; then severe diarrhœa and death. *Autopsy.* Colon and upper rectum greatly distended, especially latter and lower colon, which measured 10 cm. (4 in.) in diameter. Walls much thickened; ulceration in mucous membrane.

Hirschsprung. (*Jahrbuch für Kinderheilkunde*, 1888, xxvii. 1; *Pädiatrische Arbeiten; Henoch's Festschrift*, 1890, 78.) *Case I. History.* Boy, aged eight months. Constipated from birth; purgatives failed, and only repeated enemata produced evacuation. Constipated habit continued, and all sorts of remedies required to obtain evacuations, which were of normal color and consistence. Health good otherwise. Abdomen moderately distended; scybalæ felt in rectum; once only one stool in fourteen days. Lost health. *Under observation.* Never stool without aid; those obtained were of normal appearance. When constipated abdomen became enormously swollen, this disappearing for a brief time after opening bowels. Occasional vomiting; sound passed easily into rectum. Later unassisted movements, followed by great abdominal swelling, profuse diarrhœa, and death at eleven months. *Autopsy.* Great dilatation of sigmoid, and especially of transverse colon; wall thickened; ulcerations present. Rest of colon widened; rectum natural. No constrictions.

Case II. History. Boy, aged seven months. Constipated from birth; stool only by purgatives; no pain; no vomiting; abdomen at times greatly distended, and this gradually increased. At six months puncture with trocar. Then lost health; had diarrhœa and occasional vomiting. *Under observation.* Abdomen 56 cm. (22 in.) in circumference; peristalsis visible; profuse diarrhœa and wasting persisted until death in four or five weeks, and abdominal distention until shortly before. *Autopsy.* Great distention of sigmoid flexure and transverse colon; hypertrophy of walls; ulceration of mucous membrane.

Case III. History and observation. Boy, aged two and one-half months when he died. No stool from birth. Seen on third day, with much distended and tense abdomen. Passage of finger into rectum brought a stream of meconium out. Constipation continued, with never spontaneous stools; then more frequent stools with purgatives; then spontaneous stools; no actual diarrhœa. Abdomen always somewhat, and at times greatly, distended, with coils of intestine visible. Distention increased; health failed; no vomiting until day before death; never much pain. *Autopsy.* Distention of cæcum and ascending, transverse, and descending colon and sigmoid flexure. Hepatic and splenic flexures narrower. Walls of colon thickened; no ulceration; no strictures. Colon nearly empty.

Case IV. History. Boy, aged ten years. From the time he was little he had constipation, distended abdomen, occasionally abdominal pain usually ending in expulsion of feces and gas, exceptionally vomiting. *Under observation.* Enormous distention of abdomen; tympanitic; not tender; feces in rectum; no stool for eight days. Continued treatment with enemata produced evacuations of bowels and diminution in size of abdomen, though girth still 63 to 67 cm. ($24\frac{4}{5}$ to $25\frac{2}{3}$ in.). Had periods of spontaneous stools, not hard, sometimes thin. Six months later in fair health, but never a stool without enema.

Formad. (*University Medical Magazine*, 1892, iv. 625.) *History.* Man, aged twenty-nine years. Large abdomen and frequent constipation to one and one-half years of age. Then distention and constipation became worse. As he

grew up constipation would sometimes last a month. Abdomen increased constantly in size; tympany. Later, pain, dyspnœa, weakness. At twenty years he became a museum freak ("balloon man.") Died suddenly on water-closet. *Autopsy.* Abdomen measured 220 cm. (86½ in.). Whole colon, especially transverse, distended with gas and semi-liquid feces, measuring 25 to 76 cm. (10 to 30 in.) in circumference; no thickening of walls; no kinking or other stricture; no impaction. Rectum and small intestine normal.

Hadden. (*International Clinics*, 1893, iv. 53.) *History.* Boy, aged eleven weeks. Bowels natural until three weeks old, when symptoms began (pain, vomiting, constipation, distention) and continued. *Under observation.* Abdomen greatly distended; peristalsis visible. Treated for three weeks, then stool obtained, but child died of exhaustion. *Autopsy.* Distention of last 61 cm. (24 in.) of small intestine and of colon up to sigmoid flexure. Mucous membrane ulcerated; no stricture.

Walker and Griffiths. (*British Medical Journal*, 1893, ii. 230.) *History.* Boy, aged eleven years. Distention of abdomen noted when a few weeks of age; increased rapidly, and by three years was enormous. Bowels acted regularly until three years; then always constipation, relieved by enemata. Always dyspnœa; little pain generally; latterly more. Occasionally passage of large amount of gas relieved the distention. Died suddenly while receiving enema. *Autopsy.* Girth of abdomen 119 cm. (47 in.). Colon enormous, especially transverse and descending portion, 58 cm. (23 in.) in circumference; contained soft feces. Rectum, small intestine, and lower part of sigmoid normal. No constriction. Walls of colon much thickened; chronic inflammation of mucous membrane.

Osler. (*Archives of Pediatrics*, 1893, x. 111.) *History.* Boy, aged ten years. Always prominent abdomen; for years trouble with bowels. *Under observation.* Abdomen 63 cm. (24⅞ in.) in girth; tympanitic; not tender; some pain. Coils of intestine visible. Generally constipation, easily relieved; occasionally diarrhœa; some vomiting. Laparotomy showed "entire gut enlarged," especially the sigmoid flexure, which measured 45 cm. (17⅞ in.) in circumference. Walls much thickened; no stricture or impaction. Artificial anus made; fluid feces and gas escaped; distention entirely relieved. Recovery. No return of symptoms during several years; then lost sight of.

Mya. *Case I.* (*Lo Sperimentale*, 1894, xlviii. 215.) *History.* Girl, aged two and one-half months. Vomiting, distention of abdomen, and constipation began day after birth; stool only after repeated injections. Then tumefaction persisted, with constipation for eight days, and frequent vomiting. *Under observation.* Abdomen 45 cm. (17⅞ in.) in girth. Rectal tube passed readily. By enemata obtained passages with tolerable regularity. Seen again at eight and one-half months with return of constipation. Abdomen 53 cm. (20⅞ in.). The emptying of lower bowel, especially of gas, produced partial diminution in girth, but vomiting not entirely arrested. Child lost sight of.

Case II. History. Boy, aged five and one-half months. Twenty-four hours after birth swelling of abdomen began and constantly increased. Stools only every four or five days with enemata. Twice no stool for eight days, then vomiting and finally diarrhœa. *Under observation.* Distended abdomen, girth 52 cm. (20½ in.); tympanitic. Sound removed quantities of gas, with some diminution in size. Later developed diarrhœa, with rapid diminution in girth. Died collapsed. *Autopsy.* Large intestine everywhere thickened. Mucous membrane ulcerated. Colon irregularly distended; transverse colon most dilated, measuring 16 cm. ($6\frac{3}{10}$ in.) in diameter.

Genersich. (*Jahrbuch für Kinderheilkunde*, 1894, xxxvii. 91.) *History.* Girl, aged one and one-quarter years. No stool after birth. On second day abdominal distention began; increased greatly. First stool on eighth day of life, after purgatives, and abdomen then grew smaller. Later often long periods of constipation; occasionally vomiting. *Under observation.* Abdomen enormous, 59 cm. ($23\frac{1}{5}$ in.) in girth; tympanitic; outline of dilated colon visible; sound removed gas and lessened distention; a week before stool obtained. Later, spontaneous, soft stools, with some diminution in size of abdomen; then return of symptoms; finally diarrhœa, vomiting, and death after three months of observation. *Autopsy.* Colon much distended, 8 to 11 cm. (3 to $4\frac{3}{10}$ in.) in diameter; walls thickened; mucous membrane ulcerated. Transverse colon largest; sigmoid flexure partly distended, passing into a narrower portion. Bowel contained soft feces.

Rolleston and Haward. (*Transactions of the Clinical Society of London*, 1896, xxix. 201.) *History.* Boy, aged twelve years. Distention of abdomen began at two months. Was subject to gradually increasing constipation; often no stool for several days or even weeks, and then would be very ill and have much distended abdomen. Last two years often vomited. *Under observation.* Abdomen enormously distended; tympanitic; peristalsis visible. Obstinate constipation, with distention and abdominal distress, alternated with daily movements, with relaxation of abdomen. Hard feces in rectum at times. Watched three months. Died in one attack. *Autopsy.* Descending colon and sigmoid flexure greatly distended; rest of colon and first part of rectum less so; no stricture. Walls of colon hypertrophied; mucous membrane ulcerated.

Martin. (*Montreal Medical Journal*, 1897, xxv. 697.) *History.* Boy, aged three and one-half years. No stool until five days old. Later always constipated, sometimes going eleven days. Enlargement of abdomen began at one year, and steadily increased, with occasional lessenings following escape of flatus. Latterly slight pain. Stools scybalous; later semi-solid; two intermittent attacks of diarrhœa. *Under observation.* Great distention, girth 68 cm. ($26\frac{4}{5}$ in.). Coils of intestine and vermicular movements visible; tympanites; no tenderness; rectum normal on digital exploration. Exploratory operation done; no stricture found; wound closed. Second laparotomy two weeks later; intestines punctured by trocar; death in a few days. *Autopsy.* Perforative peritonitis. Sigmoid flexure elongated; enormously distended;

38 cm. ($14\frac{9}{10}$ in.) long, 5 to 8 cm. ($1\frac{9}{10}$ to $3\frac{1}{10}$ in.) in diameter; contained solid feces; walls thickened; no ulceration; partial narrowing of lower portion through possible thickening of mesocolon. Rectum normal. Descending colon somewhat dilated and much thickened.

The narrowing in this case does not appear to have amounted to a stenosis.

Hichens. (*Lancet*, 1898, ii. 1121.) *History.* Man, aged twenty years. Constipated "from the day of his birth until the day of his death." Abdomen always greatly distended; purgatives and enemata always needed; stools only every ten to fourteen days, and then scybalæ, followed by several loose movements. Sudden death. *Autopsy.* Abdomen enormous. Sigmoid flexure enormously distended and much elongated; 57 cm. ($22\frac{1}{2}$ in.) long, 35 cm. (14 in.) in smallest circumference; contains gas and semi-liquid feces. Walls much thickened; slight distention of colon; no stricture anywhere.

Hobbs and de Richemond. (*La Médecine Moderne*, 1898, ix. 652.) *History.* Girl, aged two and one-half years. Considerable enlargement of abdomen, giving rise to difficulty in extracting child at birth. After birth evacuation of bowels always difficult; vomiting for three months; abdomen continued to grow larger; purgatives and enemata of little effect. *Under observation.* Enormous abdomen; tympanitic. Sound entered rectum easily 25 cm. ($9\frac{3}{4}$ in.); brought away feces on its end. Puncture with small trocar allowed $3\frac{1}{2}$ litres of gas to escape, but abdomen soon filled again. Watched over a month. No improvement. Operation advised. Child disappeared.

Cases not to be included for reasons stated with each. Most of them mentioned in lists by other writers, who have not necessarily designated them as congenital.

Banks. (*Dublin Journal of Medical Science*, 1846, i. 235.) Man, aged fifty years. Had had some former attacks of same kind. This acute and fatal. No reason to consider case congenital.

Chapman. (*British Medical Journal*, 1878, i. 566.) Specimen only. Subject aged fifty-eight years. No history.

Money and Paget. (*Transactions of the Clinical Society of London*, 1888, xxi. 103.) Adult, aged fifty-five years. Clearly not a congenital case. Fatal.

Little and Callaway. (*Transactions of the Pathological Society of London*, 1851, iii. 106.) Adult, thirty-four years of age; imbecile; inordinate appetite. Died from acute constipation and overdistention of abdomen. Every reason to believe acquired.

Goodhart. (*Transactions of the Clinical Society of London*, 1881, xiv. 84.) Girl, aged seventeen years. Well until eight months before. Clearly secondary to anæmia.

Bristowe, second case. (*British Medical Journal*, 1885, i. 1086.) Man, aged twenty-four years. For "some long time" subject to constipation. No history of any congenital dilatation. Died of peritonitis.

Morris. (*British Medical Journal*, 1886, ii. 1211.) Woman, aged twenty-four years. Acute attack. Recovery. No reason to suppose congenital.

Wallmann. (Virchow's *Archiv*, xiv. 202) Man, aged sixty-six years. Several true diverticula. Not like congenital idiopathic dilatation as here understood.

Ammon. (*Angeborene chirurgische Krankheiten*, S. 39. Atlas.) Specimens from bodies of newborn or fœtus; some clearly with stenosis. No histories given, although pathologically some exhibit the characteristic lesions.

Vulpian. (*Gazette des Hôpitaux*, 1877, No. 75.) Case of dilatation, with narrow anus.

Lacave. (*Verhandl. van het Genootschap ter Bevord. der Genees en Heilkunde te Amsterdam II. Deel.* 1 *Stuck*, 1858, 7.) Clearly result of atresia ani.

Gruber. (Virchow's *Archiv*, 1872, lvi. 432.) Autopsy specimen. Probably acquired dilatation with congenitally abnormal length.

Ebers. (Hufeland's *Journal*, August, 1836, lxxxiii. 62.) Male, aged seventeen years. Symptoms rather of acute obstruction, although always constipated habit; yet no history of distention. No reason to assume was congenital.

Wells. (*Transactions of the Society for Improvement of Medical and Surgical Knowledge*, 1812, iii. 158.) Man, aged fifty-eight years. Acute symptoms; no history of previous attacks.

Lewitt. (*Chicago Medical Journal*, 1867, xxiv. 359.) Man, aged twenty-one years. First attack at twelve years. No evidence that case was congenital.

Harrington. (*Chicago Medical Journal and Examiner*, 1878, xxxvi. 400.) Man, aged fifty-one years. Acute attacks; probably old dilatation; but no symptoms of congenital affection.

Herringham and Clarke. (*St. Bartholomew's Hospital Reports*, 1895, xxxi. 57.) First case. Man, aged seventy years. Dilatation probably old, but no proof that it was congenital. Second case. Child, aged four months. Began as colitis; dilatation appears to have been secondary to this.

De Haen. (*Ratio Medendi*, iv. Cap. iii.) Quoted by Gee. Chapter III. refers to cases of drowning. Reference clearly wrong. Chapter IV. has some cases involving dilatation of colon, but none to be placed in this category.

Parry. *Posthumous Works*, vol. ii. 380.) Man, died of constipation apparently. No history of a congenital origin.

Gay. (*Transactions of the Pathological Society of London*, 1854, v. 174.) Boy, aged seven years. Condition followed an attack of typhus; probably result of this, and therefore acquired.

Eisenhart. (*Centralblatt für die innere Medecine*, 1894, 1153.) Woman, aged fifty-three years. Appears to have been an acute abdominal dilatation resulting from chronic constipation; no history of early distention.

Strahan. (*Lancet*, 1893, ii. 1245.) Man, aged thirty-two years. Lunatic. No history of abdominal distention. No reason to regard colonic dilatation as congenital.

Lespinasse. (*Journal de Médecine de Bordeaux*, 1888–1889, xviii. 427.)

Woman, aged seventy-eight years. Enormous distention of sigmoid. No evidence of congenital origin.

Favalli. (*Gazetta medica di Milano*, 1846, v. 213.) Man, aged fifty years. Acute case; no history of early distention.

Berti. (*La Pediatria*, 1894, iii. 136, 161.) First case. Seen by Porro. Congenital dilatation, but associated with imperforated anus. Second case. Child, aged thirteen months. Autopsy showed dilatation of sigmoid flexure, which may have been congenital, but symptoms entirely wanting. No constipation. No abdominal distention until last day of life. Third case. Boy, aged two months. Autopsy showed long sigmoid, with saccular dilatation of a portion of it. Appeared like a congenital malformation, but never any symptom during life. Died of marasmus.

Cheadle. (*Lancet*, 1886, ii. 1107.) Boy, aged five and one-half years. Constipated habit only for last nine months, then abdominal distention. Recovered entirely. Case apparently result of temporary atony. No reason to regard as congenital.

Osler. (*Archives of Pediatrics*, 1893, x. 111. Second Case.) Child of seven years. Supposed to be idiopathic, but autopsy two years later (personal communication from Dr. Osler) showed stenosis of sigmoid flexure.

The cases of Berti's are the only ones in this list which might with any reason be included in the first list; but as we are considering a clinical condition as well as an anatomical one it is better to exclude them from it.

A glance at the history of Roy S. and at the synopses of the published cases, a total of twenty-four in all, shows a very characteristic group of symptoms. Chief among them and first to appear are two, viz., constipation and abdominal distention. In twenty-two of the cases one or both of these was witnessed within three months, and nearly always within a few days after birth. In two cases (Bristowe's and Formad's) the time is not distinctly stated. Generally it is noticed that within a few days after birth the child tends to be much constipated. In some cases this has been complete and obstinate, and only relieved after repeated administration of purgatives or enemata. In other cases therapeutic means have been more promptly successful. In a few, as in the cases of Hadden, Rolleston and Haward, Cheadle, and in one of Gee's, several weeks or even as long as three months appear to have elapsed before the trouble with the bowels began. In Fütterer's patient there was never constipation. In nearly half the cases constipation was the first symptom noticed, although in most of these distention of the abdomen developed very soon after.

In almost all of the remaining cases the development of constipation and of distention seems to have been simultaneous. There are, however, some exceptions to this. Thus, in a few cases abdominal distention was quite late in developing. For instance, in Martin's patient and in the first of Gee's, there was no distention until the age of one year, although constipation began much before. In my patient distention was not noticed until the age of five months. In a very few cases the history seems to indicate that the development of abdominal distention has antedated that of constipation. The only certain instance of this, however, and the most marked, is that of Walker and Griffiths, in which distention was noticed at a few weeks of age and constipation not until three years. The degree of distention has varied much according to the case, but always seems to have been very marked. Frequently its degree has depended to a considerable extent upon the degree of constipation. The relief of constipation by enemata or purgatives would in most instances be attended by a decided diminution in the size of the abdomen. On the other hand, in my own case attacks of diarrhœa seemed to produce little diminution in the abdominal girth. Often nothing has given such relief to the distention as the evacuation of gas through a rectal tube. The abdominal distention was always tympanitic. Frequently the outline of the distended colon could be perceived through the thinned abdominal walls, and peristaltic movements were visible.

Particularly in the cases which have survived the first year or two of life there has been a decided tendency to repeated attacks, or rather exacerbations. In these constipation, though always troublesome and constantly growing more so, became more extreme and the abdomen more distended. With rare exceptions it has been only in such attacks that pain or vomiting has been a prominent feature. As a rule, pain and tenderness have been slight or absent, and vomiting only occasional.

As to the character of the stools, it seems only exceptional that they have been scybalous. Henoch, for instance, calls attention to the fact that the insertion of a rectal tube in his patient always brought away feces which were soft. In one of Hirschsprung's cases there had been no stool since birth, yet the finger introduced into the rectum produced the discharge of a stream of meconium.

These are examples only of the usual condition. At autopsy, too, the feces in the colon have been nearly always in a semi-liquid state. Hard, fecal masses have been the exception. In fact, everything points to an inability of the colon to propel its soft contents rather than to a blocking by hard masses.

Not infrequently there have been attacks of diarrhœa, and it is especially noteworthy that in a number of instances severe diarrhœa has been a terminal symptom.

The general health has always suffered sooner or later, although in a few instances not for a considerable time. Dyspnœa is liable to be produced by the pressure against the lungs.

It is interesting to note that twenty of the cases have been male and only four female.

The prognosis, while not totally bad, is most unfavorable. Eighteen of the twenty-four cases are known to have terminated fatally. Only three of these—those of Peacock, Formad, and Hichens—are known to have reached adult life. The remaining died in infancy and childhood—the oldest at the age of fourteen years; eleven of them before the age of five years, and six of these before that of three years. Only two patients—those of Cheadle and of Osler—can be said to have recovered, the latter consecutive to the formation of an artificial anus. When heard of some years later he was, I believe, doing well (personal communication from Dr. Osler). The four remaining non-fatal cases disappeared from observation—one of them somewhat improved, the other three not at all so.

Eighteen autopsies and one laparotomy on a case which recovered show a striking uniformity in the principal features of the pathological anatomy of the disease.

In all there was dilatation of more or less of the large intestine, generally described as "enormous." There seems to be an erroneous opinion in some quarters that it is the sigmoid flexure which is chiefly or solely dilated in this disease. I wish to call particular attention to the fact that there are but two cases described—Fütterer's and one of Gee's—in which this appears to have been the only portion of the colon dilated; and but two others—Martin's and Hichens' —in which the remainder of the colon is said to have been but slightly involved. In all the remaining, with one exception, both

sigmoid flexure and the rest of the colon were much dilated; sometimes the sigmoid flexure most (Gee, Osler); sometimes some other part of the colon most (Hirschsprung, first case; Formad, Mya, Genersich). In the one exception referred to, that of Hadden's case, the colon, without the sigmoid flexure, was involved. In a few cases the rectum was distended in a portion of its course. The small intestine was never distended to any considerable extent.

The degree of dilatation of the colon has been often enormous. It has sometimes appeared at autopsy to fill the whole abdominal cavity, crowding everything else out of sight. A very characteristic pathological feature has been the thickening of the walls of the colon. This has been reported in nearly every case. Only in Formad's is it stated to have been absent. In a few others it is not referred to (Peacock, Gee, second case). In my own case no observation was made regarding it. Generisch is disposed to regard the thickening as an early change, and as one of the causes of the loss of peristaltic power. It seems, however, just as likely—certainly in many cases—that it is a later change occurring in an effort at compensation. Ulceration of the mucous membrane is another alteration quite often seen. It is doubtless a later change, and not a necessary one. It was nearly always found in cases in which severe diarrhœa had terminated life.

The diagnosis is easily deduced from the symptoms detailed. It rests upon the very early presence of troublesome constipation; the development with this, soon after, or rarely before, of great tympanitic abdominal distention; the discovery often of the distended colon outlined through the abdominal walls; the absence of evidence that the constipation is due to impaction; the absence of any discoverable organic obstructive cause, as shown by the exploration of the rectum and colon; the absence of any previous debilitated state of health which might occasion colonic atony; and, finally, the confirmation by an autopsy that no structural obstruction of the intestine was present. This last, although of course a "post-mortem diagnosis," is often indispensable. As pointed out at the opening of this article, it is sometimes impossible—as in many other diseases—to make an infallible diagnosis without autopsy. A sharp diagnostic line between idiopathic and obstructive congenital cases cannot always be drawn.

Treatment can only be (1) hygienic and medicinal, and (2) operative. In the first class improvement of the general health is indicated, since this may help to increase the peristaltic power of the colon. Massage has been recommended by some, and condemned by others on the ground that it may produce perforation of ulcerated spots. Carefully performed in cases without diarrhœa or tenderness, it seems indicated. Electricity may be used for the same purpose. Means must be employed to empty the bowels either by purgatives or enemata. Objections exist to the use of either, since eventually they tend to weaken still further the muscular power. In the case of Hughes the child seemed to be made distinctly worse by enemata. Yet it is often a case of "needs must," and that remedy has to be selected which best unloads the bowels and gives relief. The use of the rectal tube to remove gas has sometimes been a great comfort to the patient. In three instances—Martin's, Hobbs' and de Richemond's, and one of Hirschsprung's—puncture of the intestine with a fine trocar has been performed in order to allow gas to escape.

In any severe case tending to grow worse reasonably early operation of some sort is to be advised. In spite of the gravity of the procedure, not to employ it seems still more grave. Exploratory laparotomy was performed on the patients of Fütterer and Martin, but nothing more radical was attempted. An artificial anus was made by Halsted in Osler's case, and the child recovered. The same operation was performed in my own case. Had it been done earlier, before the rapid failure of health set in, the chance of recovery would have been greater. The operation done by Treves (*loc. cit.*) on a child with dilatation consecutive to congenital stenosis might well be employed in idiopathic cases, viz., the entire removal of the functionally useless dilated colon and the joining of the small intestine with the anus. As this is a serious operation the attempt to relieve by the formation of an artificial anus may well be made first.

THE RELATION OF IDIOPATHIC DILATATION OF THE COLON TO PHANTOM TUMOR, AND THE APPROPRIATE TREATMENT OF SUITABLE CASES OF THESE AFFECTIONS BY RESECTION OF THE SIGMOID FLEXURE.

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In 1838 Richard Bright (*Guy's Hospital Reports*, London, 1838, iii. 256.) published his "Observations on Abdominal Tumors and Intumescence," in which he stated that "there is one class of cases more particularly liable to lead the unwary and inexperienced into error respecting the disappearance of an abdominal tumor; I mean cases of hysterical distention of the bowels; for although the swelling in these cases is essentially tympanitic, yet, occasionally, from the singular way in which the intestines are partially distended, and remain so for days and weeks at a time, they sometimes give completely the forms of tumors; and sometimes indistinct fluctuation may arise from fluid feces, or even from the coexistence of a distended bladder; and sometimes the large accumulation of hardened feces has led to the belief of a more solid tumor." He reported the case of a woman, aged thirty, seen many years before in Guy's Hospital, with a supposed abdominal tumor, strongly resembling an encysted tumor. "But there were connected with this supposed tumor so many other ailments, embracing fits of hysterics, epilepsy, paralysis, abdominal and lumbar pains, so varied and so changing, that a little observation was sufficient to convince any experienced person of its real character." The patient, however, again entered the hospital in 1824, complaining of abdominal pain and having hysterical symptoms. She had been seen by a surgeon who had proposed to excise the tumor which produced the swelling. A median

incision was made for this purpose, but, a tumor not being found, the wound was closed, and was not wholly healed when Dr. Bright saw the patient. Her health was in a most unsatisfactory state from a frequent tendency to diarrhœa and from a succession of pains, with occasional distention of the abdomen. She remained in the hospital some three months, during which the swelling varied considerably, and on one or two occasions was reported to have subsided entirely.

In the course of the subsequent sixteen years, as appears in an article entitled "Cases Under the Care of Dr. Addison and Dr. Gull" (*Medical Times and Gazette*, London, 1854, ix. 343), several instructive examples of the affection in question were observed by these physicians, the latter of whom is stated to have been the first to apply the term "phantom tumor." Attention was called by them to the importance of spasmodic rigidity of a part of the abdominal parietes as "one of the most frequent sources of deception. An hysterical patient is quite capable of making a circumscribed portion of the abdominal wall rigid and hard, while the rest remains comparatively flaccid. . . . The recti muscles are peculiarly apt to be the seat of these contractions, which may, however, also occur in the lateral regions of the abdomen. . . . Hardened masses of feces are probably, however, the most frequent of the exciting causes of the affection."

Later, the idea of a phantom tumor became so extended as to comprehend any circumscribed mass in the abdomen which should appear and disappear from time to time. Greenhow (*Lancet*, London, 1857, i. 58), for example, reported five cases as "Phantom Tumors of the Abdomen." The first two were apparently pedunculate pelvic tumors, the third and fourth might have been a movable kidney, while the fifth, presumably, was a movable kidney or spleen. All were regarded as spasmodic, seated "probably in the abdominal muscles, although in every instance the tumor appeared to be in the abdominal cavity." Furthermore, evanescent tumors of the trunk and of the extremities have been reported by some writers as instances of phantom tumor. Dilated and prolapsed stomachs, intermittent hydronephrosis, and transitory indurations of the mammary gland also were thus designated.

We are indebted to our honored associate, J. M. DaCosta (*Medical Times*, Philadelphia, 1871, i. 449), for a restoration of the original conception of the term and also for a most important amplification,

namely, that phantom tumors are not necessarily limited to hysterical persons. According to him, "the chief element in their production is partial contraction of the abdominal walls, particularly of the recti muscles, with more or less tympanitic distention of either the stomach or the intestine. Then a certain amount of constipation, and a large quantity of subcutaneous fat in the omentum, will modify some of the phenomena; for I do not think that all cases are precisely alike or can be explained according to an exact formula. The frequent occurrence of these phantom tumors in hysterical persons is also to be taken into account, and the co-existence with hysteria may show itself in fits of hysteria, in convulsions, or in hysterical palsy. But do not fall into the mistake of supposing any necessary connection. I have met with these tumors in men who were not very impressionable."

These views concerning the nature and the method of origin of phantom tumors have prevailed with slight modifications up to the present time. Osler (*The Principles and Practice of Medicine*, third edition, 1898, 1114) and Tyson (*The Practice of Medicine*, 1896, 1072) adopt the explanation of Gowers, according to whom phantom tumors result from a relaxation of the recti, a spasm of the diaphragm and abdominal muscles, gaseous distention of the intestine, and an arching forward of the spine. Wharton Sinkler, in the Loomis-Thompson System (*American System of Practical Medicine*, 1898, iv. 705), states that "sometimes an enormous amount of gas accumulates in the stomach and intestines, which distends the abdomen to an extraordinary extent. This condition constitutes the so-called 'phantom tumor' sometimes seen in hysteria. Constipation is frequently present, and the bowels in some cases may not be opened for weeks."

In reviewing the reports of cases of phantom tumor published in the various medical journals, it is evident that the described tympanitic tumors are by no means of uniform significance. They vary not only in extent, involving more or less of the abdominal cavity, but they vary also in duration, in severity of symptoms, and in result. Though found usually in adult females, and simulating in shape and size the pregnant uterus at full term, or an ovarian cyst, they have been observed in young girls and in men. As a rule, of long duration and of slow and gradual formation, they may increase rapidly within

a few months or within a few days. Mattison's (*Medical and Surgical Reporter*, 1863, x. 201) patient supposed herself pregnant. Menstruation had ceased, morning sickness, quickening, enlargement of the abdomen and breasts, all were observed at the proper time and in regular course. Ramskill and Jones (*Medical Times and Gazette*, London, 1859, ii. 579) state that their patient, a girl of nineteen had been several years in attendance at the Metropolitan Free Hospital. Examinations made two years apart showed no material change in the size of the tumor, which eventually caused the patient to appear like one at the full period of pregnancy. Bright's original case was observed during a period of many years in which the tumor was thought to be an ovarian cyst, and the patient was operated upon for its extirpation. Storer's case, reported by J. C. White (*Boston Medical and Surgical Journal*, 1855, liii. 19), was a girl of fourteen, in whom the tumor had been present for a year, having increased rapidly in size within eight months.

Although chronic, persisting, or recurring constipation is the rule, acute intestinal obstruction sometimes is stimulated, as is illustrated in the following case coming under my observation: In 1894 a woman, aged twenty-one years, was referred to me by Dr. W. O. Hunt, of Newton. During early childhood she had occasional convulsive attacks. At the age of sixteen or seventeen she suffered for a year from nervous exhaustion. In the two years previous to my first visit she had repeated attacks of severe pain in the lower abdomen, each lasting some ten minutes, at irregular intervals, and without obvious cause. Recently they had occurred two or three times daily, and occasionally have been associated with a discharge of blood from the rectum. Dejections were usually well-formed, and as many as two daily. There was no loss of weight or color, and there was nothing abnormal found on physical examination. Three weeks later an attack of pain was followed by an arrest of intestinal peristalsis, neither gas nor feces being evacuated, despite the use of saline laxatives and enemata. At the end of four days, during which vomiting had occurred, the symptoms of obstruction still continued. The abdomen was markedly swollen, and a distended intestinal coil was to be felt in the left half. Three pints of water were injected into the rectum without causing discomfort. A large quantity of pale urine was voided. At this time Dr. M. H. Richardson saw the case and

agreed as to the expediency of an exploratory incision. After the patient was etherized the abdomen again was palpated, when gas escaped from the rectum; repeated firm pressure caused the continued expulsion of gas, until the entire abdomen became everywhere soft and yielding to the touch. Since then there has been no return of the previous symptoms.

It is recognized that the nature of the disturbance in this case is not wholly free from doubt, but a diagnosis of hysterical tympanites seemed the most probable. It was based upon the neurasthenic, almost hysterical, antecedents of the evidently neurotic patient, whose general appearance was that of one in vigorous health; upon the immediate relief afforded by pressure when she was etherized, although all efforts without anæsthesia were of no avail, and, finally, upon the subsequent complete immunity from all abdominal discomfort.

In the diagnosis of phantom tumors of the abdomen, especial stress is laid upon their disappearance under anæsthesia. O'Donnell (*Medical Times and Gazette*, London, 1855, ii. 47) had a male patient whose tympanitic abdomen was as large as that of a woman in the eighth month of pregnancy. Under chloroform the enlargement immediately disappeared, and the abdomen for a while remained in a normal state. Simpson previously had produced the same result in like manner in a woman who supposed herself ten months pregnant. Ramskill and Jones (*loc. cit.*) also administered chloroform to their patient who, for two years, was considered to have suffered from "hysteric tympanites or phantom tumor of very large size." As the patient became unconscious the abdomen at once flattened until there was not the slightest appearance of a tumor. As the effect of the chloroform passed away the abdomen quickly resumed its previous shape, and was nearly as prominent as ever when consciousness was regained.

A notable fact in the history of this subject appears from the investigation of the periodical literature of recent years. Reports of instances of phantom tumor are rarely to be found, whereas within the past fifteen years a considerable number of cases have been published which closely simulate in their characteristics those of phantom tumor, and in which the tumor has proved to be a permanent enlargement of the colon. Little and Calloway (*Transactions Pathological Society*, London, 1851, iii. 106), to be sure, had reported previously a case of

enormous dilatation with hypertrophy of the colon, especially of the sigmoid portion, in an imbecile thirty-four years of age. The abdomen was forty-five inches in circumference at the navel, and its enlargement was found to be due almost wholly to the distended large intestine. The transverse colon was about six inches in diameter, and the descending colon and sigmoid flexure formed an immense pouch extending from the left hypochondrium into the umbilical and hypogastric regions. Peacock (*Transactions Pathological Society*, London, 1872, xxiii. 104) also described a case of fatal constipation from excessive dilatation of the colon. The patient, twenty-eight years of age, had been constipated from birth and had suffered much from flatulence. Although he enjoyed relatively good health until within six weeks of his death, the symptoms of obstruction then became grievous, and the abdomen appeared like that of a woman just previous to confinement. The large intestine from the cæcum to the upper part of the rectum was found enormously distended and contained fully fifteen quarts of semi-solid feces.

In 1884, however, Gee (*St. Bartholomew's Hospital Reports*, London, 1884, xx. 19) published his communication on "Idiopathic Dilatation of the Large Intestine," which proved to be the immediate predecessor of a considerable number of articles on the same subject. He stated that "one kind of great and fatal tympanites is an extreme dilatation of the large intestine in whole or in part. The dilatation may be called idiopathic, inasmuch as it constitutes the whole of the disease, and the foregoing conditions or causes cannot be discovered. This disease may be compared with a like dilatation, also called idiopathic, which affects the œsophagus and the stomach. . . . . At present, for want of a better explanation, I think that mere constipation and retention of wind are the cause of the dilatation." His illustrative case is that of a boy of four and a half years who was constipated when three months old, and whose abdomen continued to swell from the time he was a year old.

The purport of these publications is to maintain that increase in the size of the large intestine at times occurs without any obvious organic or mechanical cause other than fecal accumulation, sufficient to produce discomfort, distress, and deformity and to prove repeatedly the immediate cause of death. The most constant symptom is constipation, and the most positive sign is abdominal distention. Two

types of this affection are evident: in the one the disturbance begins early in life, even in infancy; in the other it becomes manifest only at a more advanced age. The former often is called congenital, although the accuracy of this term is to be questioned. To be sure, Peacock (*loc. cit.*) and Hughes (*Transactions Pathological Society*, Philadelphia, 1887, xiii. 40) state that in the cases reported by them there were increasing constipation and abdominal enlargement from birth. One of Osler's (*Archives Pediatrics*, 1893, x. 111) patients, an infant of seven months, had but five or six natural evacuations previous to having been seen by him. On the other hand, although the case reported by Walker and Griffiths (*British Medical Journal*, London, 1893, ii. 230) was observed to have an unusually large abdomen within a few weeks from birth, nevertheless the bowels are said to have acted regularly. Rolleston and Haward (*Transactions Clinical Society*, London, 1896, xxix. 201) state that abdominal swelling began in their patient at the age of two months. In Formad's (*University Medical Magazine*, Philadelphia, 1892, iv. 625) case, on the contrary, the most remarkable on record for the degree of deformity, constipation first became noticeable at the age of two years. To these cases the following is added:

A girl, fourteen years old, came under my care at the Massachusetts General Hospital in 1894, on account of a swollen abdomen. She had been constipated all her life, and the enlargement began when she was two years of age, and continued to increase in size up to the date of her admission. Three years before this there was considerable sharp, intermittent pain in the left flank, and a needle was thrust into the abdomen somewhere below the navel on the right side. No fluid was withdrawn. Otherwise she has always been in excellent health. She has attended school regularly and has seemed as strong as other children. There was no complaint of any disturbance whatsoever, with the above exception. She was well developed and sufficiently nourished. The abdomen was much enlarged, measuring thirty-one inches in circumference. It was tympanitic throughout, except in the right iliac fossa, where there was a diffused dulness. The surface was in places slightly irregular and ridged from peristalsis of the underlying intestine. On palpation the abdomen was everywhere soft and without tenderness. The bowels were kept open by enemata, and although several evacuations might occur daily there was no material diminution in the abdominal enlargement. The injection of five pints of water caused dulness on percussion in the left half of the abdomen. She remained in the hospital nearly four weeks, and several months afterward her mother wrote that there was no improvement and that she was "as costive as ever." Recent attempts to discover her whereabouts have been unavailing.

FIG. 1.

For description see case, page 24.

FIG. 2.

FIG. 3.

For description see case, page 28.

If it be admitted that in certain of the above cases a congenital cause for the dilatation may have existed, it must be recognized also that absolute evidence on this point is lacking. It is apparent, furthermore, that in some of the patients the dilatation began at such an interval after birth as to render the congenital origin very doubtful.

Mr. Treves (*Lancet*, London, 1898, i. 276), however, in a recent article entitled "Idiopathic Dilatation of the Colon," maintains that all cases of this affection "in young children are due to congenital defects in the terminal part of the bowel, that there is in these cases an actual mechanical obstruction and that the dilatation of the bowel is not idiopathic." He bases this view on the evidence furnished by a patient with dilated colon from whom he successfully removed not only the descending colon, but also that part of the bowel corresponding to the sigmoid flexure and to the rectum, which were represented by a solid-looking, though pervious, tube, eight or nine inches long, and about the size of an adult's forefinger. Support is found for his opinion in the cases reported by Dodd (*Lancet*, London, 1892, i. 1299, and Atkin (*Lancet*, London, 1885, i. 203), in which there was marked stenosis of portions of the large intestine. He offers, also, in favor of his suggestion the observations of Osler, Walker, Formad, and of Rolleston and Haward (*vide supra*).

It may be stated in behalf of those who recognize the existence of a genuine idiopathic dilatation of the colon in young children, that there are repeated instances in which the affection begins in early infancy, progresses more or less continuously, and at a laparotomy or a post-mortem examination is without sign of any congenital malformation of the bowel. Such instances are to be found even among those referred to by Mr. Treves in support of his view. In but one of Osler's cases, for example, was the opportunity offered for a satisfactory physical examination of the intestine. After an abdominal section by Halsted, although the entire colon was found enlarged and "the sigmoid flexure was twisted on itself, but not so as to cause any obstruction," no stricture of the rectum could be determined. A post-mortem examination was made in the cases reported by Walker, Formad and by Rolleston and Haward, and no evidence of a constriction was observed.

It would seem more in harmony with the facts to recognize that there are two varieties of infantile dilatation of the colon. The one is due undoubtedly to a defect of development, hence is a true form

of congenital dilatation, the result of malformation of the bowel, existing at birth and then at once producing its disturbances. The other makes its appearance within weeks or months after birth, gives no evidence of any arrest of development of the bowel, and for purposes of classification should be called idiopathic. Infantile dilatation of the colon thus may be congenital or idiopathic, but a congenital idiopathic dilatation of the colon from this stand-point would be a misnomer.

The idiopathic cases properly so called are conceivably those in which defective expulsive power is the prime factor, leading gradually to more or less abundant accumulation of feces and consequent dilatation of the sigmoid flexure, with occasional complete evacuation of the bowel, as in the case reported by Hughes, but with recurring retention extending over a prolonged period. As the lower portion of the bowel, especially the sigmoid flexure, becomes enlarged, an acquired mechanical impediment to the emptying of the descending colon, and perhaps of other portions of the large intestine, is established, giving rise to dilatation and to hypertrophy of the muscular coat. This impediment is likely to become all the greater as the loop of the sigmoid flexure becomes elongated and dilated, with its liability to kinks, even to a twist, as proved to have occurred in the case reported by Osler. In fact, the significance of elongation and dilatation of the sigmoid flexure in the production of twists of this portion of the colon is too well known to require comment. The greater the degree of distention the more impaired becomes the action of the accessory muscles of defecation, especially those of the abdominal wall, and thus may arise the enormous degrees of distention which are the eventual outcome in the cases in question.

The published instances of idiopathic dilatation first made manifest in adult life are relatively few, but may take place under the same general conditions as in this variety of the infantile series. The case reported by Little and Calloway (*loc. cit.*) was an imbecile, one of a class notoriously liable to suffer from neglected defecation. Money and Paget (*Transactions of the Clinical Society of London*, 1888, xxi. 103) state of their patient that the bowels always acted regularly, with the exception that lately they were somewhat constipated. Nevertheless, a big, scybalous mass of stony hardness was found in the colon. The patient of Herringham and Clarke (*St. Bartholomew's Hospital*

Reports, 1895, xxi. 57) is stated to have been always constipated, at times without a dejection for eight days. Richardson's patient (*Transactions of the American Surgical Association*, 1897, xv. 585), a man of forty-seven years, was in good health until the age of forty, when constipation became apparent and increased in severity. Finally symptoms of acute obstruction arose, and a half twist of the sigmoid flexure was found, corrected, and stitched to the abdominal wall. Five months later another attack of acute obstruction occurred, and again this portion of the colon was found twisted. It then was resected successfully, with subsequent relief of the symptoms.

Occasionally cases may be encountered which occupy an intermediate position between the infantile and the adult groups. I am indebted to my colleague, Dr. F. B. Harrington, of Boston, for the notes of such a case.

His patient, about forty years of age, since childhood had a distended abdomen, with constant abdominal distress and much difficulty in emptying the bowels. At the age of twenty years he had an acute affection resembling intestinal obstruction and accompanied with enormous distention of the abdomen. At this time Dr. P. Wadsworth, of Malden, treated him by plunging a trocar through the abdominal wall into the intestine. A great quantity of gas escaped, the swelling subsided, and defecation soon was resumed. Thirteen years later a similar illness occurred, but of less severity. In the subsequent seven years there were four or five such attacks, each lasting from one to four weeks, during which time the patient was confined to his bed, suffering from vomiting and intense pain. Relief followed the passage of large quantities of gas and liquid feces.

The last attack began March 6, 1898, with severe pain and vomiting, unrelieved by rectal enemata or by doses of salts. When seen a week later by Dr. Harrington, the face was pinched and haggard, the temperature 102° F., and the pulse 120. The abdomen was so distended as to resemble that of a woman with a large abdominal tumor. It was everywhere tympanitic. A median laparotomy was performed, and the cause of the enlargement was found to be the dilated sigmoid flexure, which extended from the pubes nearly to the ensiform cartilage. It was tapped, and enormous quantities of gas and fecal matter were removed. This portion of the colon was then withdrawn from the abdomen and resected. The patient lived for a week, during which time there were frequent movements of the bowels and relief from pain. Death was due to septic peritonitis of a mild grade. The united ends of the large intestine were in good condition and there was no evidence of any leakage. Dr. Harrington states, "with a similar case in similar conditions I should make an artificial anus and wait for improvement before doing a resection."

In comparing the histories of cases of chronic phantom tumor and of idiopathic dilatation of the colon the similarity in the symptoms of the two affections is beyond question. In each there is marked constipation, frequently leading to the retention of feces. In each there is a tympanitic distention of the abdomen, often of extensive degree, and present throughout a series of years, although subject to variations in size, even to a return of the normal shape in anæsthesia. In each exacerbations of abdominal distress are apt to accompany temporary increase in the size of the abdomen. The phantom tumor is not necessarily limited to persons of hysterical tendencies, and the patient with a dilated colon may be hysterical or neurasthenic. With so striking a resemblance in the clinical characteristics it seems probable that the anatomical changes are identical. Fatal cases of phantom tumor have rarely been reported. Cullen's (*Virgina Clinical Record*, Richmond, 1871, i. 153) patient died of inanition. The abdomen had been distended for five years, and the symptoms so suggested ovarian disease as to lead to the thought of ovariotomy. It is stated that no tumor was found at the autopsy, but there is no mention made of the condition of the colon. Even in the case reported by Bright, in which the interior of the distended abdomen was exposed by a laparotomy, we learn merely that no tumor was found. It is obviously inconceivable that such extreme tympanitic distention of the abdomen could exist for so long a time without the presence of gas in the intestines, and from the probability that the function of the stomach and small intestine was, as a rule, but little impaired, it seems likely that the gas must have been accumulated in the dilated large intestine. Furthermore, as already mentioned, examples of chronic phantom tumor, as described by Bright and others, are no longer reported, but cases with similar symptoms are published with satisfactory evidence that dilatation of the colon is the constant characteristic.

The following statement is added for the purpose of confirming the above interpretation of the subject:

Miss ——, thirty-seven years of age, entered the Massachusetts General Hospital in November, 1898. Since the age of fifteen, when "threatened with typhoid fever," she has been subject to periodical attacks of weakness, without obvious cause, occurring two or three times a year, rather increasing in frequency of late. The attack which took place eighteen months previous has never been wholly recovered from. During this period she has been unable to work, and has been confined to the bed a couple of months at

a time on four or five different occasions. The abdomen began to enlarge from the onset of this attack, and gradually has reached its present size. During the past year there has been more or less constant pain in the right iliac fossa, in which there is the sensation as of a lump. Of late the pain has extended upward into the right lumbar region, and in the past six weeks it has been worse than ever. For years she has been obliged to use some laxative two or three times a week, and several times a year would have no movement of the bowels for a week. The catamenia have been irregular and painful since the age of fifteen, a space of two years once having elapsed without their appearance. The interval between the successive periods may be from one week to three months. The use of the catheter is at times necessary to enable the bladder to be emptied. She has no appetite, is weak, suffers from constant abdominal pain, and attributes all her discomfort to the condition of her bowels, which causes nausea and short breath. Although there had been some loss of flesh, the face was florid, an appearance stated always to have been present. The waist was small, the epigastrium flat, but below the navel the abdomen was uniformly swollen, tense, and tympanitic to a marked degree, and measured thirty-three inches in circumference. There was diffused tenderness in the right flank. There was no alteration in the outlines of the stomach, spleen, and liver, as determined by percussion. Palpation of the region of the kidneys was rendered useless by the resistance of the overlying muscles. The pelvic examination was negative. There was neither albumin nor sugar in the urine, and the blood showed 68 per cent. of hæmoglobin, 5,616,000 red corpuscles, and 13,400 leukocytes three hours after dinner. The stomach had a capacity of twenty-five ounces of water, and its contents showed free HCl. Lactic acid also was present. When the rectal tube was inserted there was neither obstruction nor escape of flatus, nor did any change follow in the appearance of the abdominal enlargement. After the patient was etherized the abdominal walls became flaccid and the tumor disappeared, but there was no especial diminution in the circumference of the abdomen. There was merely a change of shape, the tumor-like character of which at once reappeared as the senses were recovered. There was much splashing on palpation of the region of the colon, and attempts to inject liquid and air into the bowel produced only a moderate degree of additional distention.

During the patient's stay in the hospital purgatives produced watery evacuations, but neither laxatives nor enemata caused any material alteration in the shape and size of the abdomen. She was informed of the probable cause of her condition and of the doubt of any permanent relief except by a surgical procedure of a severe and serious nature. Any reasonable attempt to enable her to resume an active life was welcomed. She was transferred to the care of Dr. C. B. Porter, who made a median incision, through which the greatly enlarged sigmoid flexure bulged. It was apparent that there was neither an organic stricture nor a fecal impaction, and as her pain had been referred to the right iliac region, and as the vermiform appen-

dix was closely attached to the abdominal wall, Dr. Porter decided to remove the appendix with the hope of relieving the pain.

This operation, speedily recovered from, gave no permanent relief, and she returned to the hospital, in accordance with my advice, for the purpose of having a portion of the colon resected. Dr. M. H. Richardson, who had succeeded Dr. Porter in charge of the surgical ward, reopened the abdomen April 5, 1899, and removed the enlarged sigmoid flexure, which represented the chief constituent of the abdominal swelling, although there was some dilatation of the rectum and the descending colon. Convalescence has progressed favorably and without interruption.

This case presented the essential characteristics, even in its reaction to anæsthesia, of a phantom tumor, occurring late in life in a woman of pronounced neurasthenic type. It likewise showed the features of idiopathic dilatation of the colon free from obvious congenital peculiarities, and having as its sole conspicuous antecedent a constipated habit, but no history of fecal impaction at any time. The phantom tumor proved to be a dilated colon.

In advocating resection of the sigmoid flexure for suitable cases of idiopathic dilatation of the colon or for chronic phantom tumor, in which the former condition presumably exists, I simply follow in the footsteps of Mr. Treves. It was his brilliant operation to relieve a patient from the effects of congenital malformation of the lower portion of the large intestine which first suggested to me the expediency of the above procedure in a case of genuine idiopathic dilatation of the colon.

The history of such cases shows that often under medical treatment the deformity and disability are permanent, generally progressive, attended by suffering and ending usually in death.

The resection of the dilated sigmoid flexure takes from the abdomen the chief cause of distention and of a fecal reservoir, which has become unnecessary, is burdensome, a source of pain and a menace to life.

It has successfully been removed, together with the descending colon, rectum, and anus, by Treves, in a case of congenital stenosis of the bowel, and the dilated sigmoid flexure alone has been removed by F. B. Harrington and by M. H. Richardson to relieve acute obstruction.

Resection may be preceded by colotomy, as in the case of Treves, and, as Harrington finds, indicated when symptoms of acute obstruc-

tion are present. Colotomy in such cases, however, should be merely a temporary expedient to relieve the patient from immediate peril and to permit him to enter into a state suitable for resection. The latter operation is best undertaken when the patient is comparatively free from all acute discomfort.

DISCUSSION.

DR. OSLER: I have some photographs here illustrating a series of cases. Two of my cases have been referred to by Dr. Griffith, and I may state the subsequent history of these cases.

In the first the operation of colotomy was performed by Dr. Halstead, and it is erroneously stated in Rotch's *Pediatrics* that the child died later. That is a mistake as far as I know, for the child was alive and doing well when last heard from, six months after the operation.

In the second case the symptoms disappeared after operation, the child improved, grew fat, and within a week after the operation for artificial anus had gained several pounds in weight. In another case I reported the child, aged seven months, lived for two years subsequently, and at the time of its death it was very much emaciated from recurring attacks of constipation and diarrhœa, and at autopsy we found enormous dilatation of the colon with narrowing of the sigmoid flexure. Just above this narrowing was a lump of concretion about the size of a hen's egg.

Another case illustrates how very few symptoms may be associated with it. A little child was brought into the surgical ward to be operated upon for knock-knees, and Dr. Bloodgood's attention was attracted to the condition of the colon. The mother gave the history that the child had not had a natural movement since birth, always requiring injections. The whole outline of the colon stood out with the greatest plainness and formed a very definite tumor that could be felt. It was hard and firm, and the waves of peristalsis were very distinct. That child is still alive.

A fourth case is a very interesting one indeed, as illustrating that this condition of dilatation of the colon sometimes disappears spontaneously. This was a boy, aged ten years, who was under my care at intervals from June, 1892, to February, 1897. He had a very great distension of the abdomen, the distention being very characteristic and the sacculation being seen with plainness through the thin abdominal wall. He had at the time of admission a chronic heart disease, and with the aggravation of this and the development of ascites the dilatation of the colon disappeared completely, so that at the autopsy there was found a thickened colon, but no especial dilatation.

A fifth case has only recently been under observation. The history dates back to within a few weeks of birth, and the three diagrams exhibited illustrate very well the condition of the colon during active peristalsis.

The very rapid improvement in the first cases after colotomy leads me to believe that the operation should be performed early, as it is a much less serious operation than that proposed by Treves, and, subsequent resection with establishment of the lumen of the gut may be made later if the first operation is successful.

DR. JACOBI: I see a great many of the cases, Mr. President, in which the diagnosis of undue length of the sigmoid flexure might easily be made from the fact that infants suffer from constipation from the first days of their lives. In a number of these cases I see a large abdomen, and have reason to believe that there is general dilatation of the colon. When the children are five, six, or seven years of age the difficulty in defecation and the size of the abdomen disappear together. On the other hand, I can well imagine, and I know that, the undue length of the sigmoid flexure has given rise to a fatal termination. I once felt obliged to operate for artificial anus in the case of a new-born with apparent imperforate intestine. Absolutely nothing was found afterward except a very long sigmoid flexure—in fact, three flexures instead of one, which compressed each other. Now, if only occasional ones terminated in dilatation, I should look for the cause of dilatation *in loco*. As there are but few autopsies recorded suggestions may be in order. There are certainly in the intestinal tract the possibilities of imperfect development of the muscular layers. I have seen that condition in the intestine only once, but met several instances in the stomach of local atrophy of the muscle; I imagine that a similar condition in the colon would give rise to dilatation.

Another cause that may be considered is the fact that the mucous membrane of the intestine in the new-born is not well formed. It contains a very large supply of more or less embryonal cells, and only gradually does the tissue become fully developed. At that time and from that cause dilatation of the colon, even without much constipation, can easily be thought of.

And, thirdly, the cause may be similar to what is noticed in rupture of the intestine. There are now about ten cases of spontaneous rupture of the infant intestine on record in which the cause was found in a more or less diffuse hemorrhage between the muscular layer and the submucous tissues.

DR. GRIFFITH: I only have to say a word about the use of the term congenital, to which Dr. Fitz has referred. When I had first written a small portion of the text of my paper I had in it a sentence to this effect, that I purposely avoided the use of the word congenital. But the more I studied these cases in detail the more was I forced to adopt the use of the term, and to employ it in the sense that it has been employed by one of the principal writers on the subject—viz., that of a congenital tendency to dilate. I think any one who will read the synopsis of the cases I have detailed will be convinced of the reasonableness of this view. Of course we

do not expect to find a dilatation present at birth, because nothing has entered the intestinal canal to produce dilatation; but when we find as soon as, or very shortly after feeding commences, a dilatation developing, not due to an obstruction, we are compelled to assume that the child for some reason was born with this tendency to dilatation. I would exclude from this category the instances of more or less globular sacs that exist at the time of birth, for this is not, strictly speaking, a dilatation, but a malformation. The affected portion of the colon has not dilated; it is malformed. I have meant to include only the cases in which the colon is, so far as we can see, natural at birth, but dilates early under any strain. Of course, whenever a child has lived a year or two without symptoms we are unable to speak of a congenital tendency, since, on the one hand, there is no reason why the symptom should not have appeared earlier with a congenital cause, and, on the other hand, we cannot show the action of later causes which would place the dilatation in the acquired class.

In regard to what Dr. Jacobi has said of the presence of dilatation from atrophy or atony, it is interesting to note that in every one of these cases in which observation regarding this point has been made at autopsy, with one exception, there has been present a hypertrophy of the walls of the colon, and that this has quite commonly involved the muscular as well as other coats. There seems to have been no atrophy in any case.

Dr. Fitz: It seems unnecessary for me to say anything further. I recognize, of course, the significance of what Dr. Griffith has stated, but we both must object to the idea of tendencies without some basis in fact for recognition. It is obvious that in many of these cases the dilatation does not begin until the child is one or two years old; rather late for a congenital tendency to make its appearance. We must draw the line somewhere, and if a child of two shows this congenital tendency what shall we say of the woman nearly thirty-five years old before the tendency to dilatation manifested itself?

One other remark in connection with the suggestion of colotomy. In my opinion, it is an operation only to be carried out in this class of cases to relieve an emergency where death threatens, or for the purpose of putting the patient in a suitable condition for resection of the dilated colon. Dr. Osler knows nothing of the present condition of his patient upon whom colotomy was performed. To go through life with an artificial anus is perhaps worse than death. The patient whose sigmoid flexure was resected at my suggestion was rendered by her ailment unable to work, and colotomy, instead of furnishing aid, would have been so much of a nusiance that she still would have been deprived of relief, hence a radical operation, the removal of the cause of the swelling, seemed to be the best plan to adopt.

A CASE OF PRESYSTOLIC MITRAL MURMUR ASSOCIATED WITH SYSTOLIC TRICUSPID MURMUR COMPLICATING PREGNANCY.

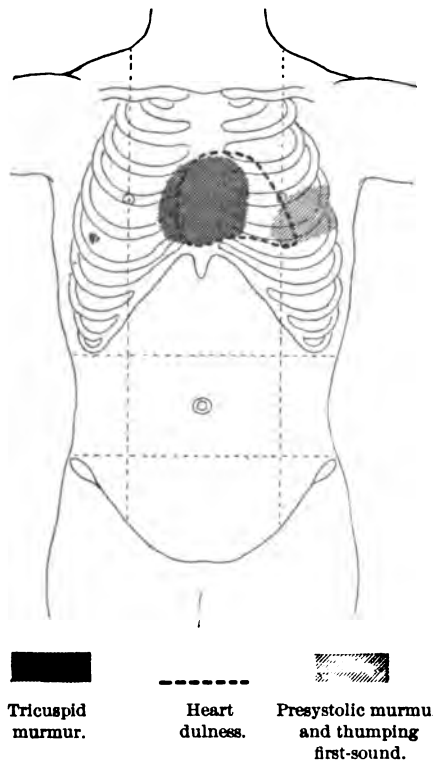
By JAMES TYSON, M.D.,
OF PHILADELPHIA.

I MAY be presuming too much to expect the members of the Association to be interested in a case of associated presystolic mitral and systolic tricuspid murmur which has been of so much interest to me, though I think few will claim that our knowledge of the presystolic murmur and its associated conditions is in all particulars complete, especially when it is remembered that some comparatively recent observers allege that the murmur is not auriculo-systolic but really ventricular systolic. I confess it was some time before I myself could recognize it as anything but ventricular systolic, and even now I often learn its true significance only through landmarks of condition and consequence by which it is, in a way, staked out for me. Further interest attaches to the case on account of the complicating pregnancy, the termination of which permitted a comparative study before and after confinement.

The patient, whose case I report, is a married woman, aged thirty-two years, who was admitted to the Hospital of the University of Pennsylvania March 16th, when about seven and a half months pregnant. She was extremely ill about eight years ago, before her first pregnancy. The illness lasted three months, and during it some operation was done *per vaginam*, but it is impossible to ascertain its real nature, and she seems to have recovered completely. Two years later she had a miscarriage. Between these two events there is a vague history of rheumatism, apparently muscular, certainly not severe. For the past five or six years she has had a winter cough which entirely disappeared in summer. For two years she has been growing short of breath, especially on exertion, has suffered much with palpitation, and has had several syncopal attacks. Three months before admission she is said to have had pleuropneumonia, and was in bed five weeks. From this illness she seems never to have entirely recovered, and although she returned

to work in a shoe factory she was compelled to give up at the end of a week. Since then she has been growing steadily worse with distressing cough and aggravated dyspnœa, often amounting to orthopnœa, growing weaker and losing weight. On admission her face was thin and pinched, while her cheeks were flushed, her eyes bright, and with her bad cough and extreme dyspnœa she looked like a consumptive. She was found, however, to be without fever, her temperature being but 97.6° F., with respiration 34 and pulse 110 per minute. Physical examination found only a general bronchial catarrh.

FIG. 1.



Inspection recognized a very striking jugular pulse connected with each systole of the ventricles, a marked systolic thrill at the apex, which was in the fifth interspace, an inch to the left of the midclavicular line. The upper border of the cardiac dulness to the left of the sternum was found in the second interspace; the right border one inch to the right of the sternum at the fourth rib. The area of cardiac dulness is shown by the dotted line in the appended drawing

Auscultation recognized at the apex a short, rough murmur terminating in a loud, thumping, first sound, presystolic in time, followed by a faint, scarcely audible second sound. When the stethoscope was carried up into the pulmonary area the second sound became rapidly intense and again less loud as the aortic area was approached, showing the accentuation to belong to the pulmonary factor of the second sound.

The presystolic murmur was not audible beyond the left parasternal line, nor was it conducted upward, although the thumping first sound was well heard in the axilla, though less loudly than in the mitral area. It was also heard less loudly at the angle of the left scapula behind. The lighter shading in the figure shows the conduction of this thumping first sound.

Just across the left parasternal line in the transverse line of apex was heard a long, loud blowing systolic murmur, more intense as the *left* edge of the sternum was reached and most intense in the fifth and sixth interspaces at this edge. It was heard upward along this edge of the sternum as high as the third rib, and across nearly so far as the right parasternal line, in fact throughout the whole of the right heart. It was not heard at the apex nor in the aortic or pulmonary areas. The dark shading indicates the space over which this murmur was heard.

Nowhere and at no time was a mitral systolic murmur audible, nor was there the irregular pulse so characteristic of mitral stenosis. Appended is a pulse-tracing which exhibits some irregularity. There was a small albumin-

FIG. 2.

uria on admission, but the urine was otherwise negative. It was extremely difficult to define the liver at its lower margin, either by touch or percussion, in consequence of the invasion of the upper abdomen by the pregnant uterus. The patient was rapidly relieved of the bronchial catarrh by potassium iodide and belladonna, and she was correspondingly more comfortable. The extreme cardiac distress was also diminished by hypodermic injections of morphine and atropine.

At 4 30 on the morning of April 11th, while the patient was asleep, the membranes ruptured, and she was awakened by the gush of water. She immediately became more comfortable, her breathing was easier and less embarrassed. Her respirations fell to 26 and pulse-rate to 90. She was transferred to the maternity department, but labor did not actually set in until forty-eight hours later. The pains were severe, but ineffectual. By noon she began to be cyanosed, and by 4.30 the cyanosis increased to lividity, when forceps were applied by Prof. Hirst and a male child quickly delivered. The relief to the cyanosis was almost instantaneous, but she was allowed to bleed freely. The pulse fell to 80, and although the breathing-rate was still unnaturally rapid her relief was inexpressible.

As soon after her delivery as seemed safe, a physical examination was made. The conspicuous jugular pulse had disappeared except a fluttering appearance, such as characterizes the false jugular pulse. The liver could now be distinctly outlined by percussion and palpation at least two fingers' breadth below the costal margin. It was tender, but not the seat of a pulsation. Before confinement the lower margin could not be found because of the encroachment of the gravid uterus. The presystolic thrill was still as plain as ever, the pulmonic second sound strongly accentuated without reduplication. At the apex, which was no longer outside of the midclavicular line, the presystolic murmur was heard as before labor, cut short by the intensified thumping first sound, followed by the faint second sound. A little further to the right, say at the left parasternal line, the tricuspid murmur comes out, is heard thence into the sixth left interspace at the edge of the sternum, and rapidly fainter toward the right edge of the sternum, where it is only faintly heard. In like manner the right cardiac border, as determined by percussion, seems not to extend as far to the right of the sternum, but it is difficult to determine because of the encroachment of the enlarged liver. The pulse had fallen to 76–80, temperature 98°, and breathing-rate 26 to 30.

When we seek the differences between the physical signs before and after delivery they are what one would expect as the result of recession of the diaphragm and subsidence of venous turgor which followed the emptying of the gravid uterus. They include disappearance of the jugular pulse, diminished intensity and conduction of the tricuspid murmur, replacement of the apex, and probably slight change in the right border. The remaining signs continued the same. There was at no time a pulsation in the left auricular region above the fourth rib to the left of the sternum, though there was enlargement of this area, as determined by percussion. The greatest strain seemed to have been on the right ventricle, and the bronchitis with which the patient was admitted also contributed to this and to its dilatation. Yet there was no œdema, notwithstanding the apparent tricuspid regurgitation. In seeking for an explanation it seems not unreasonable to account for it by the large accumulation of fluid in the amniotic sac, which may be regarded as an amniotic dropsy.

One point more deserves to be noticed—the evidence of hypertrophy of the left ventricle. In pure stenosis without regurgitation

at the mitral valve there is supposed to be no hypertrophy of the left ventricle, yet it is comparatively infrequent to find the signs of mitral stenosis without some hypertrophy. In these cases the conclusion is that there must be a certain amount of regurgitation even in the absence of a systolic mitral murmur. In the case reported the displacement of the apex after parturition was so slight that it may be inferred that the hypertrophy was not large, and that the absence of a systolic mitral murmur could be correctly interpreted as pointing to the absence of mitral regurgitation. The "thumping" first sound, characteristic of certain cases of mitral stenosis, and which was present in this case, may also be cited as evidence of sufficiency of the mitral valve, the complete closure of which seems to be indicated by it. On the other hand, the feeble second sound, so far as its aortic factor is concerned, points to an imperfectly-filled aorta and consequently feeble recoil on the aortic valve.

The very latest examination of the patient was made on April 29th, when the breathing-rate was but 20, the pulse 60, and the temperature 97.2° F., these being approximately the rates and temperature for the three days previous, uninfluenced by digitalis or other heart-tonic, as she had taken none since her confinement.

DISCUSSION.

Dr. Janeway: I would like to say a few words on mitral stenosis, for I have paid a great deal of attention to it for a long time. In the first place, the presystolic mitral murmur in about one-third of all cases can be heard behind, near the angle of the scapula. This is opposed to the rule usually stated. True, it is not as loud and not as characteristic as in front, but it is present. Sometimes we have another condition which helps us. Anyone who has had a great deal of hospital experience and has watched cases of mitral stenosis with well-characterized murmurs and has had these cases go out of the hospital and return again, perhaps to come under another service, as happens in some hospitals, will have observed that they have come in as cases of mitral insufficiency, and a great deal of uncertainty has been brought about in this way: that when the autopsy was held mitral stenosis was found where the clinical history gave mitral insufficiency. I have watched such cases for years, had them go out of hospital, return later, and though there was no doubt that at first they were cases of mitral stenosis, the condition was otherwise when readmitted with enlarged liver, swollen limbs, and perhaps considerable œdema. When, however, later the liver became reduced in size, the dropsy disappeared, and the heart had become sufficient again,

then with a returned presystolic murmur there was again no doubt of the nature of the process. When death, however, resulted shortly after admission to the hospital with dropsy, etc., and only a mitral systolic murmur, has the difficulty of explaining or comprehending the relationships of murmur to mitral stenosis been introduced.

A stranger murmur I have seen this year, occurred with a dilated pulmonary artery, but the thrill, instead of being at the apex, was where you would expect a thrill in cases of pulmonary stenosis. The thrill and murmur were so placed as to make it appear a case of pulmonary stenosis instead of mitral stenosis.

DR. CAREY: So far as the change of location of the clearest point of hearing a presystolic murmur is concerned, I would like to raise the question with Dr. Janeway as to whether its transmission behind may not be accounted for by the more or less pulmonary consolidation. I would not like to use the word in the sense of absolute consolidation, but may it not be a transmission through a lung more or less altered by consolidation, making the murmur more or less constant? There is no doubt in the world but what cardiac sounds are often better heard in unexpected places if there is furnished a temporary solid means of transmission. I am of the opinion, too, that it is rare that you get a deformed auriculo-ventricular orifice which could produce an obstruction sufficient to give rise to a presystolic murmur and also an auricular dilatation, but would not give rise to more or less valvular leakage, and, as Dr. Tyson said, although the ventricular murmur may not be distinctly heard, it is almost certain that there could not be a stenosis without regurgitant leakage.

DR. GRIFFITH: I am very glad to hear Dr. Janeway speak as he has. Four years ago I read a paper before this body, in which I recorded seven cases of mitral stenosis which had been under observation within three months, in all of which the murmur was heard very much beyond the limits ordinarily stated, and in some cases in the back. That this had occurred so frequently in my own experience in such a short time convinced me that it must be of common occurrence and must certainly be frequently observed, yet the text-books said almost nothing about it. Nearly all gave the same stereotyped description of the usual area. I must except some of the older books, among them the works of Walsh and Hayden, which do distinctly refer to this wide difference.

DR. TYSON: The point made by Dr. Janeway is one which I think clinicians now generally recognize, especially since attention has been called to it by Dr. Griffith's paper. This fact remains distinctive, however, of the presystolic murmur that, while it may be conducted to the axilla and sometimes behind, it always remains very much loudest at what may be called its proper site, that of the apex. This is not so literally true of other murmurs, especially of the aortic diastolic, which is heard all over the thorax, often with great loudness, and its point of greatest intensity is not always at the aortic orifice.

A CASE OF MITRAL STENOSIS, WITH FEVER, (NON-MALARIAL) OF RELAPSING TYPE.

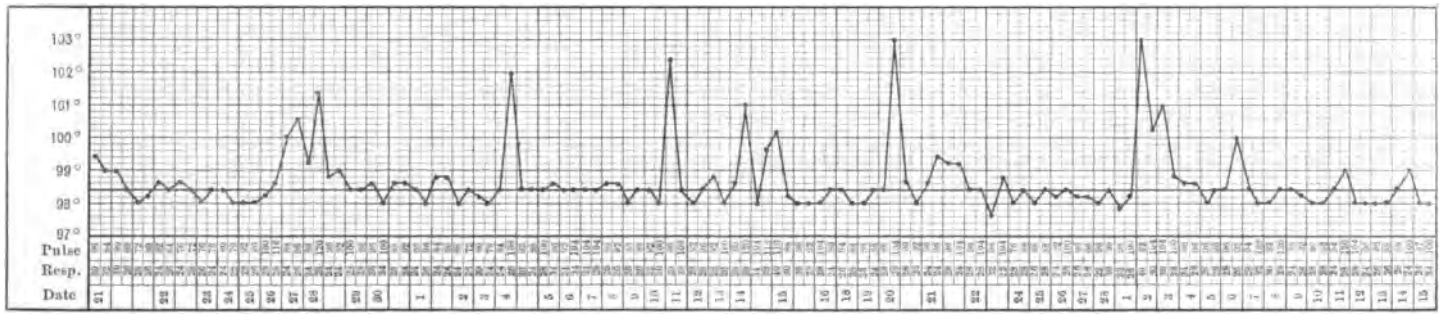
By FREDERICK P. HENRY, M.D.,
OF PHILADELPHIA.

THE title of this report is open to criticism, inasmuch as the fastigium of relapsing fever continues for a period of several days, whereas in the case I am about to discuss the acme of the fever was maintained for but a few hours. In employing the adjective relapsing I mean to imply a fever *recurring* at intervals of about one week, and, so far as I am aware, such a type of fever, in connection with endocarditis, has not been hitherto described. In a paper entitled "The Chronic Intermittent Fever of Endocarditis"[1] Osler reviews the literature of the subject, mostly English, and finds one of the earliest references to it in Ormerod's Gulstonian Lectures, which were published in 1851. In this case there were two febrile paroxysms daily, and in all the reports with which I am acquainted the type of fever has been either quotidian, tertian, or, as in Ormerod's case, double quotidian. The rarity of the febrile type presented by my case has seemed to me sufficient warrant for its publication.

Margaret D., aged nineteen years, dressmaker, admitted January 21, 1899. Father living and well at the age of sixty-eight years; mother died at the age of thirty-two years of pneumonia. Has had four brothers and three sisters of whom one brother and two sisters are living. The patient had typhoid fever three years ago; rheumatism in childhood; pneumonia a few months ago. She has lived in Philadelphia all her life.

Present Illness. About ten days before admission she began to feel weak and languid and disinclined to work, with headaches, pains in the back of the neck and back, and poor appetite. In addition there was anorexia, occasional nausea and vomiting, soreness in the abdomen, epistaxis, diminished excretion of urine, and cough. The menses have been suspended for two

[1] Practitioner, 1893, vol. *i.* p. 181.


103°
102°
101°
100°
99°
98°
97°
Pulse
Resp.
Date

months. The patient is a fairly well nourished white female of average height. Her face is flushed, expression dull, eyes half closed, tongue lightly coated and tremulous; pulse 96, respirations 30, temperature on admission 99.2° F.

Physical examination revealed nothing abnormal except a typical presystolic murmur, low pitched, prolonged and rumbling, followed by short, sharp, first sound, the second sound being scarcely audible at the apex. The heart is but little if at all enlarged, the apex-beat being palpable in the fifth intercostal space within the mammary line.

On the day after admission the temperature became normal, and so continued until the 26th, fifteen days later, when it began to rise. On the 28th, at 8 P.M., it reached 101.4° F.; on the 29th it was again normal, and remained so until February 4th (six days later), when it suddenly rose at 8 P.M. to 102° F. Six days later, at 6 P.M., there was another ascent to 102.4° F. On the 20th it again rose at 8 P.M. to 103° F., slighter elevations having occurred on the 14th and 15th. On March 2d (at 8 A.M., it again suddenly rose to 103° F., after which it continued normal.

The accompanying chart shows the character of the febrile movement much better than any verbal description. On two occasions the rise of temperature was accompanied with a chill, and in one with the vomiting of undigested food. Repeated examinations of the blood for the malarial organism gave negative results. The urine was free from albumin, sugar, and casts, and the liver was of normal size and apparently healthy in all respects. It is scarcely necessary to add that foci of suppuration were carefully excluded.

On March 25th the patient was examined in the clinic by my hospital colleague, Dr. Edward P. Davis, with special reference to the question of pregnancy. Dr. Davis concluded that the woman was pregnant.

The blood was examined on three occasions, the average of the three counts giving 2,705,000 red corpuscles per c.mm. and 20 per cent. of hæmoglobin. The leucocytes numbered 6000 per c.mm. A differential count of the latter was not made.

To recapitulate: The patient is a young, unmarried woman, pregnant, highly chlorotic, with well-marked though well compensated mitral stenosis and fever, which may be styled recurrent, relapsing, or intermittent, but is certainly not malarial. The inference that the fever is dependent upon the heart lesion is based on the fact that no other cause for it could be found. This is the basis upon which rests the universally accepted opinion that the more regular types of intermittent fever and the continued fever associated with endocarditis are dependent upon the latter.

So far as I am aware, no theory has been advanced to explain the intermittency of non-malarial fever, such as that attending hepatic

disorders, tuberculosis, endocarditis, etc. In discussing these intermittent fevers, it should, I think, be borne in mind that in health there is a diurnal variation of the temperature, and that, as I demonstrated in the Cartwright Essay for 1881, diurnal elevation is coincident with a diminution in the number of the red blood-corpuscles and an increased elimination of urinary pigment—in short, that it corresponds with hæmolysis. As first pointed out by William Hunter, the occasional elevations of temperature in pernicious anæmia are also hæmolytic, as evidenced by their coincidence with a deeper discoloration of the skin, an excessive elimination of pathological urobilin, and a still further diminution in the number of red corpuscles. The condition, in short, is an exaggeration, or, rather, a perversion of what obtains in health. The intermittency of the malarial fevers is also coincident with a parasitic invasion and destruction of the red corpuscles; and with these facts to guide us I would suggest the probability of solving the problem of non-malarial intermittency by a careful study of the blood.

It might be suggested that the fever of my patient was due to the impoverished state of the blood; in other words, that it was the same in kind as the so-called anæmic fever of pernicious anæmia. In reply to such a supposition I would call attention to the fact that the characters of the blood were those of chlorosis, the percentage of red cells being more than double that of the hæmoglobin, and that febrile chlorosis is rarely met with. According to Huchard also, fever, when it occurs in chlorosis, is continuous.[1] It might, with equal, propriety, be argued that the anæmia is the result of the valvular affection, for, as is well known, in endocarditis, especially of the ulcerative form, the anæmia is often intense. I recall a case of ulcerative endocarditis which I saw with the late Dr. James H. Hutchinson, in which the anæmia was so profound that the cardiac murmur (mitral systolic) so soft that the diagnosis for a time vacillated between pernicious anæmia and ulcerative endocarditis. At the autopsy the left auriculo-ventricular orifice was almost occluded with vegetations, and most of the viscera contained numerous emboli.

The fact that my patient is still living and at present free from fever is no argument in favor of the view that this symptom was not etiologically connected with the valvular disease, but was due to some

[1] Sajous' Annual Univ. Med. Sciences, 1891, vol. ii.

undiscovered ephemeral cause. I have purposely refrained from using the term "malignant" as applied to endocarditis, because I know of no dividing line, either clinical or bacteriological, that can be drawn between malignant and benign forms of that disease. The view that an ulcerative endocarditis is necessarily fatal is also disputed by Leyden,[1] who relates two cases of apparent recovery from that condition.

The sole criterion of malignancy in cases of endocarditis is their fatal termination after an acute febrile attack, which may be intermittent, continuous, or, as in the case just reported, recurrent or relapsing.

DISCUSSION.

DR. DOCK: The suggestion that the febrile paroxysms in this case are due to some process in the blood is interesting, but does not explain the whole process, nor explain the cases where there are two paroxysms a day, as in the cases reported by Ormerod, by myself, and by Dr. Thayer.

DR. W. W. JOHNSTON: It seems to me the explanation of these cases must be found in what we know to be the cause of analogous conditions in malarial fever, namely, the life-history of an organism. In septic endocarditis, acute tuberculosis, malarial fever, etc., we must conclude that the intermittent fever is due to phases in the life of a parasite.

I arose more particularly, however, to show a chart of a case of some little interest. The patient, a young woman of about twenty years, was taken ill with fever while in the country, and was under the care of a good physician and a trained nurse. She had throughout the illness no symptom except some gastro-intestinal dyspepsia, with a peculiar run of fever. She had no symptoms that pointed to typhoid fever, though that was at first suspected. The fever consisted of recurrences of a regular form, at regular intervals. For instance, she had a fever for eight days, then a period of eight days without fever. This was followed by eight days with and eight days without fever. Then fourteen days of fever, ten days without; eight days with fever, fourteen without; and finally, ten days with fever. So that there was a certain regularity about the recurrences. The blood was examined very carefully and nothing found that would throw any light upon the condition. It was certainly non-malarial, and no method of treatment seemed to have any effect. Gradually the recurrences ceased. I do not remember to have seen a temperature record exactly like this. (Exhibiting temperature-chart.)

[1] Ueber intermittirendes Fieber und Endocarditis. Zeitschrift für klin. Med., 1882, No. 4.

DR. THOMSON: There is certainly the presumption raised that the condition of intermittency is more or less connected with the life-history of some micro-organism, yet I published a case a year ago of insanity which has been constantly under observation for five years, and where the disease has lasted for nine years, in which the gentleman becomes periodically worse every other day. He has never been known to miss that feature in his history. The exacerbations come on about one hour before awakening—about five o'clock in the morning—and he remains in a very nervous state for the day. When he first came under my observation these exacerbations were attended by a rise of temperature. He had been treated and his blood examined repeatedly for malarial organisms, but no such thing found. For the past four or five years when the exacerbations appear the temperature has remained normal. Now in that case it is difficult to account for the condition upon the supposition that he is infected, and it seems more like a nervous phenomena.

DR. HENRY remarked, in closing the discussion, that the suggestion that the fever in his and similar cases might be hæmolytic, did not exclude the operation of micro-organisms, but rather implied it, inasmuch as the type of all periodic fevers (ague) is both hæmolytic and parasitic.

CONCERNING KERNIG'S SIGN IN MENINGITIS.

By JAMES B. HERRICK, M.D.,
OF CHICAGO.

In 1884 Kernig,[1] of Russia, described a phenomenon which he thought was found only in affections of the pia mater, and which was never lacking in inflammations of that membrane. If a patient with meningitis be made to sit up, as on the edge of the bed, the thigh, therefore, being at a right angle with the body, it is found extremely difficult to extend the leg, because of the presence of a marked flexor contracture. To quote Kernig: "The phenomenon is so striking, the difference between nothing and something ('zwischen Null and Etwas'), between the complete absence of the contracture while the patient is lying down, and its presence when the patient sits up is so plainly perceptible that it is well worth while to pay special attention to this symptom and to examine for it in every case."

Kernig saw 15 cases of meningitis, in all of which he found the symptom. In 8 cases there was confirmation of the diagnosis by autopsy. Of the 15 cases, 13 were epidemic cerebro-spinal meningitis, 1 tuberculous, 1 suppurative. Kernig failed to find the sign in many diseases other than meningeal affections. In 6 cases, however, where there was not acute meningitis, the sign was more or less marked; yet in all these he found some pial trouble—œdema, intermeningeal hemorrhage, circumscribed meningitis, chronic meningitis, general carcinosis. Kernig believed the sign appeared in meningitis as early as the rigidity of the neck, and that it is late to disappear.

Kernig's sign seems to have attracted comparatively little attention for fourteen years. Most of the standard text-books on nervous diseases make no reference whatever to it. Some authors describe the phenomenon, but disclaim any individual responsibility for the correctness of the statement by bracketing Kernig's name after the

[1] Kernig: Berliner Klinische Wochenschrift, December 29, 1884.

statement (*e.g.* Oppenheim). Still others state briefly that it is rarely found. "A peculiar, but as it appears extremely uncommon, symptom, is the so-called flexor contracture of Kernig." (Hirt, p. 14.) Until Netter, in 1898, revived interest in the subject there are, so far as I can discover, but four writers who recorded the results of their clinical observations on this phenomenon, Bull (1885), Henoch (1886), Friis (1887), and Blümm (1889).

Bull[1] wrote to show that the sign was not pathognomonic of meningitis or even of pial trouble, but merely indicated an increase in intracranial pressure. He found the flexor contracture in three cases, one of tuberculous meningitis, with no autopsy, one of solitary tubercle of the cerebellum, but "in the pia over it a few miliary tubercles," with tuberculosis in lung, lymph glands, kidney, and intestine; one of otitis media with caries of petrous portion, thrombosis of transverse sinus and common jugular. In the basal pia, especially over the frontal lobe, were ecchymoses, and there were a few teaspoonfuls of serum in the posterior fossa. These cases, it seems to me, go rather to prove Kernig's statement, that his sign is found with affections of the pia mater, than Bull's, that it is not indicative of meningitis or even involvement of the pia. For on Bull's own showing, one of his three cases was tuberculous meningitis, another had miliary tubercles in the meninges, the other certainly some local meningitis with numerous ecchymoses and an unusual amount of serum.

The most extended observations are those of Friis,[2] of Copenhagen. During an epidemic of cerebro-spinal meningitis, the examination for Kernig's phenomenon was made in 60 out of 110 cases. In 53 of the 60 the sign was present, *i.e.*, 88 per cent. In 2 of the remaining 7 it was doubtful, in 2 the examination was unsatisfactory, in 3 the sign was absent. Friis was unable to state how early it appeared, or how late it remained. He found no relation between it and stiffness of the neck, hyperæsthesia or pain, though he was inclined to think it was more pronounced where lumbar pain was most complained of. Friis has no explanation to offer as to the cause of the phenomenon, but does not agree with Bull in regarding it as due solely to intracranial pressure as he has seen it absent in a case of hydrocephalus.

[1] Eduard Bull: Berl. Klin. Woch., 1885, No. 47, p. 772. Ueber die Kernigsche Flexionscontractur der Kniegelenke bei Gehirnkrankheiten.

[2] Albert Friis: Om den i Kjobenhavn i Aaret, 1886, Herskende Epidemi af Meningitis Cerebrospinalis. Thesis, 1887, p. 154.

TABLE I.—SHOWING CASES OF MENINGITIS EXAMINED FOR KERNIG'S SIGN.

No.	Date.	Name, age, sex.	Where seen.	Day of disease.	Clinical symptoms.	Kernig's phenomenon.	Result.	Autopsy.	Remarks.
1	Sept. 30, 1898	..... adult, F.	C. C. Hospital, Dr. Preble.	?	Fever, delirium, rigid neck, swollen joints, paralysis of some of ocular muscles.	Marked.	Died.	Pneumococcus septicæmia, with suppurative arthritis, pericarditis and meningitis	
2	Oct. 7, 1898	? adult, color'd, M.	C. C. Hospital.	12th	Old cough, slightly dull at one apex, chest elsewhere hyper-resonant, emaciation, cyanosis, rapid respiration, fever, delirium; T.B. in sputum. Diagnosis: miliary tuberculosis. On Oct. 5th, no rigidity of neck and no Kernig; on Oct. 7th, neck rigid and retracted, and Kernig pronounced.	Marked; can lift patient from bed without the knees yielding in extension.	Died.	No autopsy.	Of interest to note absence of Kernig at first, but appearance later as evidence of meningeal involvement became marked.
3	Oct. 16, 1898	R. adult, M.	Drs. McNeal and Heywood.	8th	Headache, vomiting, temp. 99–102°, delirium, insomnia, involuntaries; no spleen; neck rigid, facial paresis; no evidence of syphilis, no benefit from iodides.	Present.	Died.	No autopsy.	Meningitis, probably tuberculous.
4	Oct. 30, 1898	..... Adult, color'd, M.	C. C. Hospital.	?	Fever, semicoma, rigid neck, right ptosis, etc. Diagnosis: Tuberculous meningitis.	Present.	Died.	Autopsy: tuberculous meningitis.	
5	Nov. 15, 1898	Willie, 10 yrs. M.	C. C. Hospital.	9th	Headache, delirium, later coma; strabismus, rigidity and retraction of neck, unequal pupils, papillitis, temp. 99–101°, herpes labialis.	Present.	Died.	Autopsy: meningitis.	Nature of meningitis not determined bacteriologically; probably epidemic.
6	Dec. 2, 1898	..... adult, M.	C. C. Hospital.	?	Alcoholic and syphilitic; headache, thick speech, rigid neck and jaw, involuntaries, emaciation, cyanosis, rapid respiration. A micrococcus in smears from lumbar puncture.	Present.	Died.	Autopsy: syphilitic meningitis with acute process superadded.	

7	Dec. 6, 1898	M. 48 yrs. M.	C. C. Hospital.	?	Brought in unconscious; temp. 101°, hyperæsthesia, rigidity of neck; diplococcus by lumbar puncture; mind clearer after lumbar puncture.	Marked.	Died.	Autopsy: cerebro-spinal meningitis.	
8	Dec. 17, 1898	W. 4 yrs. F.	Dr. Pigall.	14th	Prodromal irritability, headache; five days ago convulsion; later rigid and retracted neck, and coma; pupils unequal; Cheyne-Stokes respiration, emaciation, patellar reflexes slightly exaggerated.	Not present, or very slight	Died within a few hours after examination.	No autopsy.	Diagnosis: tuberculous meningitis.
9	Jan. 11, 1899	..... 25 yrs. F.	Dr. Urheim.	7th	Empyema one year before; operation; two later operations, but sinus still remaining; for several days headache, bewilderment, delirium, temp. 100°; no rigid neck or paralysis at time of examination.	Present.	Died two days later.	No autopsy.	Probable tuberculous meningitis secondary to primary pleural tuberculosis.
10	Jan. 16, 1899	S. 3 yrs. M.	Dr. McCullough	8th	Influenza, pneumonia, suppurative otitis; for about four days stupor; temp. 100 to 104°; constipation, retention of urine; neck retracted and stiff; lung still consolidated; no paralysis, but great laxity of all muscles; only by severe pinch or firm supra-orbital pressure can even a slight turning of the hand be produced; no patellar reflexes.	Not present in right leg, in left very slight.	Died 20 hours after examination.	No autopsy.	Pneumonia, metapneumonic otitis and meningitis.
11	Feb. 20, 1899	B. B. 27 yrs. F.	C. C. Hospital.	Several	Two years ago nursed husband with consumption; one year ago pleurisy. Before admission severe headache and convulsions, delirium, strabismus, retinitis, retracted neck, "ganglion" on hand; lumbar puncture negative; cyanosis, rapid respiration, tender abdomen, temp. 99-102°.	Present.	Died.	Autopsy: old tuberculous pleurisy, solitary tubercles in brain, with general miliary tuberculosis; some small tubercles in meninges.	
12	Feb. 22, 1899	..... adult, M.	C. C. Hospital, Dr. Billings.	Several	Sore-throat, headache, delirium, herpes, petechiæ, retracted neck, diplococcus intracellularis from cerebro-spinal fluid; coma on eighth day.	Marked.	Died.	Autopsy: epidemic cerebro-spinal meningitis.	
13	Feb. 26, 1899	S. 17 yrs. F.	Dr. T. E. Roberts	17th	Tuberculous family history; prodromal irritability of temper; headache, becoming extremely severe and constant; temp. for 17 days 99-103°; delirium, retraction of neck, variable pulse, ptosis, Cheyne-Stokes, coma, rapid pulse; no spleen, spots or Widal.	Present in lt. leg; in rt. leg, by constant, gentle force, the leg straightens out, giving way with a sort of snap.	Died, 56 hours after examination.	No autopsy.	Diagnosis: tuberculous meningitis.

No.	Date.	Name, age, sex.	Where seen.	Day of disease.	Clinical symptoms.	Kernig's phenomenon.	Result.	Autopsy.	Remarks.
14	Mar. 22, 1899	A. L. 8 yrs. M.	Presb. Hosp., Dr. Cotton.	20th	Headache, vomiting, delirium, rigid neck, coma, variable pulse; temp. 99–103°+; leucocytosis (22,000); lumbar puncture negative; great emaciation.	Present continuously from Mar. 22 to May 2.	Recov., with deafness.	.....	Diagnosis: epidemic cerebro-spinal meningitis
15	Mar. 24, 1899	V. 25 yrs. F.	C. C. Hospital, Dr. Roberts.	7th	Headache, tender and rigid neck, muscular twitchings, tâche cerebral, delirium; temp. 100–104°; lungs, heart, etc., negative.	Marked.	Died.	No autopsy.	Diagnosis: meningitis, probably epidemic.
16	Mar. 24, 1899	W. B. adult. M.	C. C. Hospital, Dr. Preble.	?	Coma, restless, rigid neck, slight ptosis; temp. 103–104°, pulse 66–88, albumen; an abundant diplococcus by lumbar puncture.	Marked; Kernig also present just before death, though not as marked as day before.	Died.	No autopsy.	Epidemic meningitis.
17	Mar. 25, 1899	C. R. 41 yrs. M.	C. C. Hospital, Dr. Billings.	?	Headache, slight rigidity of neck, stupid even to falling out of bed, involuntaries; temp. 98–100°; diplococcus by lumbar puncture.	Present.	Recov.	.....	Diagnosis: meningitis, probably epidemic.
18	Mar 26, 1899	Geo. S. color'd, 30 yrs. M.	Dr. F. B. Earle.	29th	Onset with headache, vomiting; delirium, retracted and rigid neck, pulse rarely over 100, temp. 97–104°, involuntaries, resp 24–34; no cyanosis; leucocytosis; no plasmodia; no Widal.	Present.	Recov.	.....	Epidemic cerebro-spinal meningitis; on May 1st, there was no Kernig present; patient able to walk.
19	April 2, 1899	N. 2½ yrs. F.	Dr. Pigall.	3d	At first feverish, wanting to lie down; mother thought "bilious" and gave oil; next day convulsions and fever, stupor, "gritting of teeth," jerkings, coma, eyes half open, left eye reddened and with muco-pus on globe, neck rigid when attempt is made to move it, and whole body then quivers; temp. 102°+; pulse 160, respiration irregular, lungs negative.	Present.	Died, in 12 hrs.	No autopsy.	Meningitis, probably epidemic.

In an epidemic in Copenhagen in 1891 Friis[1] found the sign in 21 of 26 cases (80 per cent.).

Henoch,[2] in 1886, reported on the Kernig sign. His later views can be gathered from his reference to it in his *Kinderkrankheiten*, seventh edition, page 320. He has found the Kernig contracture present in many cases of meningitis, but does not regard it as pathognomonic, as he has in at least one case with autopsy found no contracture. And he thinks it may be present without meningitis.

Blümm[3] found Kernig's sign in 7 of 9 cases of meningitis.

Last year, 1898, Netter,[4] in examining 25 cases of meningitis, found Kernig's sign present in 23 (92 per cent.), some cases abortive, others advanced, 2 convalescent; 8 cases were tuberculous, 3 mixed tuberculous and epidemic, 12 epidemic. One of the exceptional cases was a child seen but once, the other a child living at the time of communication, with evidences of advanced tuberculous meningitis. Netter believes its presence permits one to assert quite positively the existence of a meningitis. He regards it as of especial value in the diagnosis of abortive types of epidemic meningitis. From its persistence into convalescence (Kernig, Henoch, Netter) it may be of service in enabling one to make a retrospective diagnosis.

A still more extended experience with 47 cases is reported by Netter.[5] He found the test positive in about 90 per cent. of cases of meningitis.

My own observations have been made upon 19 cases of meningitis, with autopsy in eight cases. All doubtful cases have been excluded. Nine were epidemic cerebro-spinal meningitis, 7 were tuberculous, 2 were pneumococcic, 1 was syphilitic with an acute process superadded. These cases, for convenience of reference, have been arranged in tabular form. I take this opportunity of thanking the physicians who gave me the opportunity of examining some of their patients, and in particular Drs. Billings and Preble, who courteously extended to me the freedom of their wards at the Cook County Hospital.

[1] A. Friis: Ugeskrift for Laeger, 1892, pp. 407 and 431, cited by Netter.

It is interesting to note that in studying these cases Friis found and described an intracellular diplococcus evidently the *intracellularis*. His figure on page 27 of his thesis is an excellent representation of the specific organism. He does not, however, declare it to be the specific germ, though questions its identity with Fraenkel's pneumococcus.

[2] Henoch: Charité Annalen, 1886, p. 575.

[3] Blümm: Münch. Med. Woch., June 25, 1889.

[4] Netter: La Semaine Médicale, 1898, p. 281. Clinical lecture delivered at Hôpital Trousseau.

[5] Bulletin et Memoires de la Société Médicale des Hôpitaux de Paris, Juli 22, 1898. Abstract in Deut. Med. Woch., January 26, 1899.

From the table it will be seen that Kernig's sign was present in 17 out of 19 cases of meningitis, or in 89.4 per cent. In the 2 cases in which it was absent, both children, the single examination was made a short time before death, and it was noticed at the time that there was a general laxity of all the muscles; in the one case there being but the faintest movement of an arm in response to firm and long-continued supra-orbital pressure. This recalls the fact that even the retraction and rigidity of the neck muscles may be variable, and just before death may entirely disappear. "In patients deeply comatose, and shortly before death, I have frequently seen the stiffness of the neck disappear."[1] Kernig's sign may have been present earlier. Friis states that it may vary in degree from day to day. In most of the cases examined the other signs were so unequivocal as to make the examination for the Kernig phenomenon wholly unnecessary, except as a confirmatory finding. In some of the cases, however, its presence was of distinct value from the paucity of the commoner evidences of meningitis, *e.g.*, in Cases III. and IX. And in Case II., one of miliary tuberculosis, it was of especial interest to note the absence at first of Kernig's phenomenon and its later appearance at the same time when evidences of meningeal involvement were first manifest—retraction and rigidity of the neck, severe headache, paralysis of ocular muscles.

Netter,[2] in a footnote, cites an extremely instructive case showing the value of the Kernig phenomenon, to which reference may here be made. In a typhoid with typical symptoms, including the agglutination test, Kernig's sign was marked. But from the absence of other pronounced meningeal symptoms meningitis was excluded. Death occurred in the third week from perforation. The autopsy revealed typhoid and also a cerebro-spinal meningitis due to the staphylococcus pyogenes and the bacillus typhosus.

Many patients with diseases other than meningitis were examined as to the existence of Kernig's phenomenon, there being selected as many cases as possible in which there were cerebral symptoms. Many individuals of all ages who were in apparently perfect health were examined. In 25 healthy individuals selected at random no Kernig sign was present. In 100 cases of disease other than meningitis, Kernig's sign was absent in 98, present in 2. The result is shown in the following table:

[1] Eichhorst: iv. 473, Fourth edition.

[2] Netter: La Semaine Méd., 1898, p. 282.

TABLE II.—SHOWING CASES OTHER THAN MENINGITIS EXAMINED FOR KERNIG'S SIGN.

No. of cases examined.	*Diagnosis.*	*Kernig's phenomenon.*
25	Healthy individuals from infancy to old age, both thin and fleshy	Absent.
5	Pneumonia	"
3	Convalescent pneumonia	"
2	Pneumonia with delirium tremens	"
5	Delirium tremens	"
1	Tetanus; fourteen days after injury, trismus, convulsions, fever, mild delirium	"
2	Uræmia	"
3	Malaria	"
1	Convalescent malaria	"
3	Typhoid fever	"
5	Cerebral hemorrhage	"
1	Cerebral thrombosis	"
3	Cerebral syphilis	"
1	Tumor of brain	"
1	Subdural hemorrhage (autopsy)	Present.
1	General paralysis of insane	Absent.
1	Multiple sclerosis with spasticity	"
1	Ataxic paraplegia	"
2	Convalescent multiple neuritis	"
1	Tabes and hysteria.	"
2	Hysteria	"
1	Incipient Graves's disease	"
2	Lead poisoning	"
1	Opium poisoning	"
1	Influenza with cerebral symptoms	"
1	Pernicious anæmia	"
2	Chlorosis	"
1	Enteroptosis	"
4	Acute rheumatism	"
4	Chronic rheumatism	"
1	Gonorrhœal rheumatism (vide text)	Present.
10	Valvular disease of heart	Absent.
1	Fibrous myocarditis	"
1	Acute endocarditis	"
5	Carcinoma of stomach	"
2	Ulcer of stomach	"
3	Asthma and bronchitis	"
1	Mastitis	"
1	Chronic nephritis	"
1	Amœbic dysentery	"
6	Pulmonary tuberculosis	"
1	Pelvic inflammation	"
1	Facial erysipelas with delirium, vomiting, high fever, headache, etc.	"
1	Loose body in knee-joint	"
1	Chronic gastritis	"

In a case of Dr. Billings, Kernig's sign was present where post-mortem a subdural hemorrhage was found with no inflammatory changes.

The patient was a laborer, aged fifty-two years. Headache and forgetfulness for a few days. Found unconscious, having apparently fallen out of bed. Rigid and retracted neck, equal pupils, right facial paresis, right arm flexed and rigid. Involuntaries. Temperature on admission normal, but in twenty-four hours up to 104°, with pulse 130. After lumbar puncture temperature 98°, pulse 56. Later temperature but slightly elevated; pulse variable. Mental condition varied from coma to quite bright intelligence. When rational, no rigidty, no Kernig sign. When comatose, Kernig's sign present.

Died in coma on fourteenth day. Autopsy revealed subdural hemorrhage, left side.

It was present in the unaffected leg in a woman who had been lying in bed for four weeks with a gonorrhœal arthritis of one knee. During this time she had lain with both knees flexed, as this was the most comfortable position. This local condition may explain the difficulty experienced in making extension in the leg so long accustomed to flexion.

The absence of the sign was of diagnostic value in the case of facial erysipelas. The patient, an adult, went to work in the morning feeling nearly as well as usual, and returned at noon complaining bitterly of headache and nausea. "He staggered into the house like a drunken man." By 3 P.M. he was delirious, and his physician found a temperature of 104°, with, he thought, some stiffness of the neck, and diagnosed meningitis. When I saw him next day there was still complaint of severe pain in the head; he had not slept the night before; was slightly delirious; temperature 103°. Other findings, in lungs, heart, abdomen, muscles, negative, save that breathing through the nose was difficult, as the nose seemed "stuffed up" as from a cold. There was no Kernig sign, though the patient, a fleshy man, and his wife both said they knew he would be unable to extend the leg as he sat on the edge of the bed, as he had tried it many times in his efforts to put on his shoes and stockings. In one leg extension was made with some little difficulty, but still sufficiently easy to exclude Kernig's phenomenon, a strong argument, it seemed to me, against meningitis. The next morning the nose and adjacent skin of the face showed typical erysipelas, and the case was clear, though the prevalence of sporadic cases of epidemic meningitis made one at first seriously consider the possible existence of this affection.

From the study of cases made by Kernig, Henoch, Friis, Blümm, and Netter, with the observations just recorded, it seems justifiable to regard Kernig's phenomenon as present in the majority of cases of meningitis—say 80 to 90 per cent.—and as only exceptionally present in other affections. Other and more definite conclusions concerning it seem unwarranted at present. That it may occasionally be absent in meningitis and occasionally present in diseases other than meningitis, should not cause it to be wholly discarded as of no value. The truly pathognomonic symptoms are few. Rose-spots in typhoid, herpes in malaria and pneumonia, absence of free hydrochloric acid in carcinoma of the stomach, murmurs in endocarditis, choked disk in cerebral tumor, and scores of other symptoms are not pathognomonic, but rightly deserve attention when found or when absent, as helping to make up or modify the symptom-complex of a disease, the method of diagnosis upon which, as yet, clinicians are compelled largely to rely.

As to the technique of eliciting this sign, it is exceedingly simple. The patient may be made to sit up on the edge of the bed with legs hanging down, thus bringing the thigh at right angles to the body, when extension of the leg can be attempted. Or the thigh can be brought at right angles to the body as the patient lies in bed on the side, or preferably on the back, and the leg then extended. The only requirement seems to be that the thigh should be placed at a right angle with the body before the attempt is made to extend the leg. Not infrequently in delirious patients, *e.g.*, in delirium tremens, there must be a little patient, gentle force used before the jerking and tense muscles yield. The same is true of some spastic conditions. But where Kernig's contracture is present, patience and gentleness do not cause the muscle to yield, and the back of the patient can generally be lifted from the bed without the knees giving way. This procedure is often accompanied by evident pain to the patient. In some cases the leg and thigh will make an obtuse angle of no more than 110° or 120°. As Kernig says, the test in many cases is most striking, particularly in those patients whose thigh and leg in the recumbent position are extended and apparently lifeless, but in the test position reveal a most intensely rigid contracture, often with evidence of acute pain. In testing for Kernig's sign there must be excluded those cases in which local causes could interfere with the proper extension of the leg, such as rheumatic or other form of arthritis of the hip or knee, myositis, old contractures from nervous diseases, and sciatica. The phenomenon can be well-imitated by the latter condition.

No thoroughly satisfactory explanation of this phenomenon has been offered. Bull's notion that it is merely an evidence of increased intracranial pressure is disproved by the many failures to find the sign in hydrocephalus, in tumors, and in hemorrhage. His notion is further, that it is but an exaggeration of a normal condition. Even in health it is often somewhat difficult to secure easy and complete extension of the leg with the thigh flexed at right angles with the body, owing to the tenseness of the muscles at the back of the thigh. Henoch[1] aptly cites the statement of Landois, that the flexors of the leg springing from the tuber ischii are too short to permit of free extension of the leg when the thigh is flexed on the body at an acute

[1] Loc. cit.

angle, and he further calls attention to the fact noted by Henke,[1] that owing to the shortness of their muscular fibres and the abundance of tendinous fibrous material, the semi-tendinosus, semi-membranosus, and biceps femoris are unable to stretch far enough to permit of complete extension of the leg when the thigh is sharply flexed on the body. It is easy to assume, therefore, that in meningitis there is such an increase in tone as to exaggerate this natural difficulty of extension into a contracture of the flexors of the leg. But just how this is brought about is a matter of speculation.

DISCUSSION.

DR. OSLER: I can speak of the presence, even of the value, of this sign in the epidemic of cerebro-spinal fever. In a number of cases we have had recently it has been present in a very marked degree. I do not know that in any single instance it has been a help in the diagnosis, as the condition of meningitis was readily recognized from the presence of other symptoms. I can understand, though, that in other cases, particularly of typhoid fever with marked cerebral symptoms, or the cerebral type of pneumonia, that this sign may be of great value. It is certainly a very interesting sign, and the experience of Dr. Herrick and others shows that it is present in a very large percentage of cases.

DR. GRIFFITH: I have neglected to look for this sign as often as I should have done in the last winter, but I may state that so far as I have examined it was nearly always present in meningitis, and that I have not seen it in other conditions. Just before leaving home I tested it in two cases of cerebro-spinal fever, and found it well marked in both. One of these children might have led one astray in diagnosis very readily. It was an obscure case, and if it had not been for the history of a family epidemic the diagnosis would have been most difficult. In similar cases, but without the aid of such a history, I can see that the presence of Kernig's sign would be of great help.

[1] Henke: Hand Atlas, Berlin, 1888, i. 175.

THE CONTINUED FEVER OF EPIDEMIC INFLUENZA.

By WILLIAM W. JOHNSTON, M.D.,
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THAT the fever of influenza sometimes assumes a continued type of long duration has been recognized and described by Leveran in 1889–90 (*La Medecine moderne*, 1889–90, p. 143), and some of its descriptive characters pointed out; Moretti (*Il Raccoglitore medico*, 1891, serie v. 12), Lemoine, and Wörner have devoted attention to the subject. Hollister, of Chicago, in 1892 (*Journal of the American Medical Association*) reported 50 cases observed in hospital, with an average duration of twenty-three and a quarter days. But the literature of the subject is not large, and nowhere have I seen any satisfactory description of the symptoms most frequently met with.

The statements here made are based on a number of cases observed during the past two winters, and in all essential particulars the uniformity of symptoms is so great as to make it possible to give a more or less definite description of this variety.

The onset of fever is sudden, as in all cases of influenza; sometimes a short, acute catarrhal stage is followed by prolonged fever, of which the slight catarrh is only an incident. More frequently the attack is of the mildest character in its beginning, so much so, indeed, that the patient makes the futile attempt to fight off illness without a physician's aid; for a week he rises daily, and perhaps goes to his business, but progressive weakness and increasing fever finally force him to seek help.

By this time the fever has reached 101° to 102° in the evening. The further course varies, but not within wide limits. As a rule, the evening temperatures are ascending for two to five days, the morning remissions corresponding to the elevations, and ranging from one to two degrees. The fastigium, with temperatures of 102° to 103°, lasts

from three days to one week or ten days. Defervescence is gradual, resembling typhoid, or is more rapid and irregular. The normal point is reached at different dates. In the three charts shown it was on the fourteenth, sixteenth, and twenty-first days respectively.

The oscillations in Case I., up to the twenty-first day, give a total curve exactly resembling enteric fever. In the other two cases the irregularities are greater than in this disease.

When the fever reaches a point at or near normal it is by no means over, and the patient may be very far off from convalescence.

In Case I. after the twenty-first day, and between that date and the thirty-ninth day, the temperature did not get below 99° in the morning, nor below 100° in the evening, once reaching 100.8°, and once 101.2°.

From the thirty-ninth day the temperature range was nearer the normal, but at no time was the normal point reached in the evening until after the sixty-seventh day.

In Case II., between the sixteenth day and the fifty-fourth day, when the record ends, the morning temperature was at or near normal, but the evening temperature was 101° or over during the first week, and later 100°, and never below 99° during the last week. There was an evening rise for twenty-eight days, and perhaps longer, after the continued fever had ceased.

In Case III., from the fourteenth day, when the more continued fever seemed about to end, until the one hundred and fourth day, when observations were no longer made, there was a continuance of fever of a low grade, remittent and intermittent by turns, ranging from normal to 101°.

While the earlier part of these curves bears more or less likeness to enteric fever, the latter part is unlike the temperatures of the defervescence and convalescence of that disease.

The common characteristic of the latter stages of influenza fever is the long-continued minor oscillations and very delayed disappearance of the evening rise, long after patients have resumed an active life.

That this peculiarity does not belong only to influenza fever, without lesion, is shown by the fever of the late period of influenza pneumonia. In Case IV. the temperature is shown of a case of catarrhal pneumonia, with bloody sputum, after the disappearance of

all acute symptoms. During sixty-two days the evening temperature stood at an average of 99.5°, frequently reaching 100°.

There is no acute infectious disease in which this peculiarity of delayed disappearance of fever exists, under the same form of regularity, as in influenza. Prolonged fever in infectious diseases is due to complications, and has variations which depend upon the rise and decline of such complications; but in influenza a daily intermittent fever of low grade is a part of the disease, and must be considered as an essential feature of the symptomatic picture.

THE SYMPTOMS in cases of this description are very uniform. Careful and repeated examinations fail to show any pulmonary, pleural, pericardial, or endocardial lesion. The catarrhal feature disappears, or is so slight as to admit of no relation between it and the fever. There may be a slight cough only, or none throughout.

In Case II., during the first week of illness, the symptoms were headache, pains in the limbs, slight cough, ringing in ears, and some deafness, occasional rigors, and profuse perspiration. During the second week there were pains in the limbs and side, nausea, a feeling of faintness and prostration, breathlessness, feeble and intermittent pulse.

In the third and fourth weeks there were nervousness, dyspnœa, insomnia, and mental depression; the heart's action was more feeble and intermittent, and the sense of prostration greater.

The improvement from the end of the fourth week was slow, the patient leaving her bed for the sofa for the first time on the fifty-third day of the illness. She sat in a chair for the first time on the sixty-first day. Convalescence was slow from this time, the patient feeling feeble during the spring and summer, having dyspnœa on slight exertion. At this time, a year since her illness, she has regained flesh, but complains of oppression in the region of the heart after mounting steps. There are no signs of any lesion of the heart.

In Case III. the prominent symptoms were violent muscular pains in the thoracic wall, pains in the limbs and back, nausea and irritability, insomnia, mental depression and anxiety, profuse sweats, little or no cough. At the end of the fourth week the heart's action became rapid, feeble, and irregular, and from this time this became the chief symptom. The feeling of exhaustion was very great, and the dyspnœa with the feeble heart-action made his condition at times

alarming. Improvement was very slow. He left his bed for the first time on the fifty-fifth day of his illness, and sat up for a few moments on the sixty-third day. Slight exertion was followed by a feeling of faintness and by feeble and intermittent pulse. He drove out for the first time on the seventieth day, and left the city a few days later. One month after this he was stronger. At that date, August 6th, there was still an evening rise of temperature. Strength has never been completely regained since his illness. During the past winter he has suffered from bronchitis and asthma, and is now out of the city for this reason.

The two features that are the most striking in cases of this kind are the long continued and characteristic fever-curve, with the marked cardiac symptoms.

Influenza affords a good example of the long residence in the body of infecting micro-organisms. Pfeiffer, Wasserman, Beck, and Kruse have repeatedly found influenza bacilli in the sputum for weeks and months after an attack.

In a case of pulmonary influenza, accompanied by great induration, Netter found the presence of Pfeiffer's bacillus in the expectoration during fourteen months. In chronic fibroid pneumonia, also, Pfeiffer has demonstrated the presence of the bacillus lasting for a long period.

The long duration of fever and of other symptoms is due to this peculiarity of influenza infection, a persistence of effect that is more decided than in most of the acute infections.

The heart symptoms are probably due to some alteration of the myocardium, as well as to the effect of infection on the nervous centres.

Weichselbaum found fatty change in the heart muscle in a number of cases. A peculiar form of "cardiac grippe" has been described by Huchard; slowing of the pulse, with great rapidity on sitting up, irregular or intermittent heart action, and pain resembling angina pectoris are given as symptoms. These symptoms were all present in the two cases referred to. The question is whether myocardial change is not the constant and only essential lesion of the form of influenza characterized by the fever and symptoms described. The feeble pulse noted in these cases, as well as in others, prolonged for a year or more, is an evidence of a lesion due to the attack. In

Case II. the heart sounds, now one year after the illness, are indistinct, the impulse feeble, and the respiration disturbed by slight exertion or mental excitement. In other words, the symptoms are those of cardiac dilatation, which may be presumed to be due to degeneration of the heart muscle at the time of the acute illness. The changed state of the nervous system since then would justify the theory that the symptoms were neuropathic, if it were not for the physical signs of constant heart weakness. This condition could only result from a change in the myocardium itself, a change that may be progressive and in any case, is chronic.

DIAGNOSIS. The recognition of the nature of a fever of the type described must be sometimes difficult, as mistakes are often made. It is sometimes taken for enteric fever, or for acute tuberculosis.

From enteric fever the distinction is easily made, if attention is paid to the mode of onset and to the more characteristic symptoms that are not like those of enteric fever. I have never seen the so-called typhoid forms of influenza, nor any cases in which the diagnosis could not easily be made. The differential diagnosis cannot be based upon the fever-curve, but upon concomitant symptoms; and sooner or later the difference in physiognomy, and the presence of myalgia and neuralgia, with the heart feebleness and irregularity, point conclusively to influenza. In any case the peculiar intermittent terminal stage makes its nature plain.

From tuberculosis the diagnosis may be difficult for a time if there are any fine unilateral râles, but the subsequent fever oscillations exclude tuberculosis sooner or later. The intermittent fever stage is entirely unlike tuberculosis in the low evening elevations and in the tendency to improvement after the fourth or fifth week.

TREATMENT. A word only will be said about treatment. The guiding rule is to keep the patient alive until the infection wears itself out. The heart claims most attention, as it involves the chief danger to life. But the greatest suffering comes from the state of the nervous system; insomnia, nervous agitation, mental depression, neuralgia, and muscular pain call for relief. And for these there is no remedy but morphia given in small doses, continuously for days or weeks, if need be. No matter how much opposed one may be to the remedy, its use is forced upon us by the character of the suffering and by its long duration. Morphia not only relieves this, but it is the most efficient aid

in sustaining the action of the heart. It can be given in minimum doses, repeated at intervals as necessary, increasing on occasion, and then gradually reduced as the need disappears.

The patient being entirely under our control, there is no danger of the morphia habit being created. He can be cured at will of whatever dependence he may have acquired.

SOME REMARKS ON TYPHOID FEVER AMONG OUR SOLDIERS DURING THE LATE WAR WITH SPAIN.

By VICTOR C. VAUGHAN, M.D.,
OF ANN ARBOR, MICH.

In August, 1898, Surgeon-General Sternberg appointed a board consisting of Major Walter Reed, U. S. A., Major E. O. Shakespeare, U. S. V., and the writer to study the causes and the spread of typhoid fever among the troops in the various camps within the United States. In accordance with this order the members of the board have been and are still engaged in this investigation. Although our work is, as yet, incomplete, and our conclusions may be somewhat modified after we have collated and compared more figures, we are apparently justified at present in formulating certain conclusions which may be of interest to the profession. With the approval of Surgeon-General and of my colleagues on the board I am permitted to present to you some of the facts that we have learned, with conclusions which, in our opinion, are justified by these facts.

It may be well, in the first place, to say something concerning the methods which we have pursued in our investigation of this subject. In accordance with the instructions given us by the Surgeon-General we visited and carefully inspected all the larger encampments in the United States, including Camp Alger, the camps at or near Fernandina, Fla., Jacksonville, Fla., Huntsville, Ala., Chickamauga Park, Ga., Knoxville, Tenn., Wycoff, N. Y., and Meade, Pa. In making this inspection, to which we gave about six weeks of time, we endeavored to ascertain by direct personal observation the conditions under which the soldiers lived. We visited nearly every regiment at each of these camps, made ourselves acquainted with the water supply, the quality and quantity of the food, the preparation of the food, the nature of

the soil of the camp, the space allotted to regiments, the arrangement and size of the tents and the number of men occupying each tent, the location of sinks with reference to the mess tents, the disposition of fecal matter and garbage, the thoroughness with which the camps were policed, etc. We visited regimental, division, and other hospitals, and ascertained the methods of disinfection practised in these hospitals. In short, we endeavored to see for ourselves everything that might have a bearing on the origin and spread of typhoid fever. While making this inspection we took the testimony of medical and other officers. We hoped to be able to interview at least one medical officer in each regiment, but this was not always possible. However, the information that we obtained in this tour of inspection was considerable, and some of it of much value.

Since finishing the inspection we have been engaged in studying the records in the office of the Surgeon-General. In this study, also, we have regarded the regiment as the unit. We have endeavored to ascertain when typhoid fever first appeared in each regiment, and how it afterward spread. How many cases there were in each company. If one or more companies furnished an unusually large number of cases, we have endeavored to ascertain whether or not the men in these companies have lived under unusual conditions. Thanks to the courtesy and intelligence of some of the regimental medical officers, we know how many men in each tent had typhoid fever and the initial date of each case. In our complete report we hope to give all this data, but in this paper I must content myself with general statements, substantiated by a few details.

We had not finished our first day's work at Camp Alger before we saw that one factor in the problem must be thoroughly dealt with before we could hope to reach a satisfactory solution. Fortunately, we promptly took steps to acquaint ourselves with this factor. It cannot be denied that scientific medicine would have gained much had this factor been provided for at an earlier date. I refer to the question of the scientific diagnosis of typhoid fever. In the division hospital at Camp Alger we found most of the febrile cases diagnosed as malarial. We believed that they were typhoid fever, but the surgeons in charge had diagnosed them malaria. We requested that competent men, properly equipped for making blood examinations for the malarial plasmodium and the Widal test, should be sent to each

of the larger camps. The Surgeon-General acted promptly on this suggestion. Drs. Gray and Carroll, of the Army Medical Museum, went to Camp Alger for this purpose. Subsequently Dr. Carroll continued this work at Jacksonville. Dr. Dock, of the University of Michigan, made investigations at Chickamauga, Knoxville, and Meade. Acting Assistant-Surgeon Craig also spent several weeks in making blood examinations at Sternberg Hospital, Chickamauga Park. Dr. Curry, Acting Assistant-Surgeon at Fort Meyer, has made many hundreds of blood examinations upon sick soldiers sent from Camp Alger, Jacksonville, and other camps. As a result of the work done by these men, we are able to state that malaria was a very rare disease among those troops who remained in the United States. Among the hundreds of blood examinations made on soldiers from Camp Alger, not one case of malaria was found at that place. Dr. Dock found one case at Chickamauga and one at Meade. The one at Chickamauga was a private of the 2d Arkansas Volunteer Infantry, who stated that he had had chills and fever at home in the spring of 1898 before he enlisted. The malarial case at Camp Meade belonged to one of the Pennsylvania regiments. Two weeks before the examination of the blood this man came, so he stated, from a camp on the banks of the Potomac. It will be seen, therefore, that in each of these cases the plasmodium was probably introduced into the system elsewhere than at one of the large camps.

Malaria was probably more frequent than these figures indicate, but that the long-continued fevers diagnosed as malaria in nearly all the field hospitals were typhoid fever there can be no doubt. The sick reports contain evidence in themselves that malaria was not a prevalent disease among the troops. The 158th Indiana, 6th Ohio, and 1st West Virginia constituted at Chickamauga Park one brigade, and were encamped side by side. According to the sick reports malaria prevailed in the Indiana regiment from May throughout the summer. There were no cases in the Ohio regiment in May; 3 in June; 11 in July; 103 in August, and 203 in September. In the West Virginia regiment malaria does not appear on the records until August, when 108 cases are reported. That there could have been malaria in the Indiana regiment in May and not a case in either of the other regiments in the same brigade, is not probable; and that it would have taken this disease two months, had Chickamauga been the

fearfully malarious place it is said by some to be, progressing slowly through the Ohio regiment, to reach the West Virginia regiment, is not in accord with any known epidemiological facts concerning this disease. Pushing our inquiry further, we find that in the Ohio regiment 273 individuals are recorded as having had malaria. Sixty-six of these were sick only a few days. Among these there may have been a few cases of malaria, but the probabilities are that even for these diagnoses of febricala would have been quite as scientific. Of the 207 cases of protacted malaria, 148 were still sick when the last report consulted by us was made (October 31, 1898). This leaves 59 cases of completed malaria, among which there are reported 12 deaths. A death-rate of more than 20 per cent. in "mild remittent malaria," as the disease is designated by one of the surgeons, is, to say the least, unexpectedly high.

To summarize concerning the so-called protracted malarias reported by the regimental surgeons, I will say that, in my opinion, practically all of these were typhoid fever, and the following are my reasons for this opinion:

1. The uneven distribution of the so-called malaria among regiments encamped side by side gives cause to suspect that these cases were not malaria.

2. Some of the surgeons who failed to record their cases as typhoid state in their comments that typhoid fever prevailed in the regiment. One illustration of this may be of interest. From April to November there were in the 6th Ohio, according to the recorded diagnoses in the monthly reports, only two cases of typhoid fever. Notwithstanding this fact, the acting assistant-surgeon in charge at that time writes in the October report the following statement: "The health of the command is improving. The prevailing disease that has caused the sickness we have had is typhoid fever." And yet the September report showed only one case of typhoid fever, and the October, report showed only one case, and this one case was one and the same patient carried from the August report on to the reports for September and October.

3. The results of several hundred blood examinations showed that malaria was a very rare disease among the troops that remained in the United States.

4. Malaria as it exists in this country is easily controlled by mod-

erate doses of quinine. All the so-called protracted malarias in our camps were treated with large doses of quinine, and were not improved thereby. Consequently, we must conclude that the diagnosis given in these cases was erroneous.

5. The mortality of the so-called protracted malarias corresponds with the mortality of typhoid fever, and furnishes most positive proof that these cases were not malarial.

When we began to study the regimental sick reports we found that, in order to obtain satisfactory information, we must endeavor to ascertain how many cases of typhoid fever there were in each regiment, and it soon became evident that the regimental sick reports did not give this information. Of two regiments in the same brigade, one had more than 200 cases of typhoid fever, as shown by the regimental reports; while the other regiment on like evidence had only two cases, but the records of the second regiment show more than 200 cases of protracted malaria, and these furnished a mortality as high as that of the typhoid fever in the first regiment. For the reasons already given, we have included all the protracted malarias among our list of the typhoids. It may be asked how long we have considered it necessary for a so-called malaria to run in order to make it a probable typhoid. In answer to this, I will state that we have regarded all so-called malarias of ten days or more in duration as possible cases of typhoid fever. We think that the great rarity of true malaria and the readiness with which these rare cases have yielded to quinine, and the fact that quinine was so generally administered, justify us in this conclusion. Practically, however, the number of doubtful cases is exceedingly small.

Typhoid fever was not only diagnosed malaria, but it was covered up by many other names. In one regiment the death-rate from prolonged indigestion amounted to 15 per cent. of the completed cases. In another regiment at Chickamauga dengue is a frequent diagnosis of many cases which undoubtedly were typhoid fever. That dengue should have prevailed in one regiment among the 60,000 troops at Chickamauga is too absurd to receive serious attention. By tracing all doubtful cases to the hospitals we have been able to reach a positive opinion concerning the nature of most of them. In some regiments we have made an alphabetical list of all the sick. In others we have taken only those who are recorded as having had some intestinal

disorder, malaria, or some form of continued fever. In some regiments many cases were diagnosed simple continued fever. In others the surgeons seemed to regard enteric fever as distinct from typhoid fever. The belief of some of the medical men in typho-malaria is evident by their reports.

The origin of typhoid fever in all the larger encampments is easily determined. Many of the volunteer regiments and some of the regular regiments were infected with typhoid fever when they reached the camps. A few illustrations are interesting. The 6th Ohio reached Chickamauga Park May 18th with a case of recognized typhoid fever. This patient was kept in the regimental hospital until he died, May 24th. The 9th New York arrived at Chickamauga May 26th. There was a suspiciously prolonged case of diarrhœa June 10th, and one of enteric fever three days later. The 31st Michigan arrived May 17th and furnished a recognized case of typhoid fever June 1st. The 1st Arkansas reached Chickamauga May 27th and sent a probable typhoid case to the division hospital June 2d and a recognized case of typhoid fever June 3d. The 52d Iowa came May 31st, and the surgeon recognized a case of typhoid fever June 8th. The 1st Missouri went into camp at Chickamauga May 21st and had a suspicious case May 31st. The 5th Missouri came May 27th and furnished a suspected case June 6th. The 2d Kentucky arrived May 26th and, so far as the records show, had no typhoid fever until June 26th. The 2d Missouri arrived May 20th and furnished a probable case May 26th. The 12th New York came May 20th, and the first suspected case had its initial date ten days later. The 1st New Hampshire arrived May 22d, and two days later entered on its sick report a case that was most probably typhoid fever. The 8th New York arrived May 25th, and did not show any evidence of the existence of typhoid fever until June 24th. However, as this patient died July 1st, it is probable that the true initial date was earlier than is indicated. The 2d Ohio arrived May 18th, and two days later a case diagnosed as gastro-enteritis, and which may have been typhoid fever, was treated in the regimental hospital. These are not selected regiments, but these data were taken from a bundle of records at hand at the time of this writing, and each record in the bundle was examined.

It is safe to say that more than 90 per cent. of the volunteer regiments that went to Chickamauga Park reached that place infected

with typhoid fever. So widespread is typhoid fever in this country that in assembling a regiment of volunteers the probabilities are that one or more men in the regiment will be found to be infected with this disease. Medical officers might do well to bear this in mind, and be on their guard for the detection of the first case of typhoid fever. Instead of doing this, many medical officers will refuse to recognize typhoid fever until it assumes epidemic proportions, and the records that we have studied show us that often when typhoid fever has become an epidemic some medical officers refuse to give the disease its right name, and prefer to call it something else. This aversion to calling typhoid fever by its right name seems to exist among medical officers in all armies. The German medical officer calls the disease "gastric fever," and this term appears now and then in our records when the surgeon happens to be a German. The French call it "manæuver fever." I am inclined to the opinion that medical officers often are led to suppress the diagnosis of typhoid fever for fear of the alarm that it will give the patient and others. This, however, is a mistake. We will not eradicate this disease from our camps until we recognize its presence and take proper steps to prevent its spread. Typhoid fever in a camp should be reported at medical headquarters and to the medical officers of other regiments, as diphtheria in a school should be reported.

It may be well to emphasize the fact that our troops carried in their own persons the typhoid infection to the encampments. Some acquired the disease at the State encampments, and others brought it directly from their homts. In one of the Alabama regiments typhoid fever was at first confined to one company, and this company came from a town where there was an epidemic of the disease at the time when the men enlisted. From this company the disease spread through the regiment.

The next question is: How did typhoid fever spread among the troops? In answering this inquiry we quite naturally first direct our attention to the drinking water. So far as our studies have been carried up to the present time the evidence concerning water infection is, for the most part, negative. There is no evidence that the general water supply at the larger encampments was infected with typhoid fever. At Jacksonville the general water supply to all the regiments was from artesian wells a thousand feet deep, and infection of this

water seems well-nigh impossible. Moreover, in round numbers, there were at Jacksonville last August and September 30,000 soldiers and about the same number of residents. Both soldiers and citizens used the same drinking water, and yet there was a widespread epidemic of typhoid fever among the soldiers and only a few sporadic cases among the citizens. At Knoxville the soldiers and citizens used drinking water from the same source, and at the time of our inspection, September, 1898, there were hundreds of cases of typhoid fever among the soldiers, and the records of the health officer showed no evidence of the existence of the disease among the citizens. Some of the regiments at Chickamauga drank water from the creek, which might have been contaminated. These regiments suffered from typhoid fever; but other regiments which had no water from Chickamauga creek and which brought their supply a long distance from mountain springs, the contamination of which is highly improbable, had typhoid fever just as badly as did those who drank water from Chickamauga creek. There is another very interesting point in this connection. The three regiments of a brigade are encamped side by side, water from the same pipes is distributed alike to all these regiments, and yet typhoid fever has prevailed for twenty days and has become epidemic in one of these regiments, while one of the others remains wholly free from the disease. A similar condition is observed when we study the distribution of the disease among the companies in a regiment. I think that we have found evidence of water-infection at some of the minor camps, and it is probable that soldiers while off duty and out of camp drank from infected wells, but we are quite confident that the general water supply of the larger camps was not infected and that water-infection played a very subordinate rôle in the spread of typhoid fever among the soldiers in the camps in this country.

All know that the specific bacterium of typhoid fever is eliminated from the bodies of those sick with this disease in the urine and feces, especially in the latter, and that the disease is transmitted from one person to another by the transference of some part of the feces from the sick to the alimentary canal of the well. It follows that the spread of typhoid fever will depend upon the disposition of the excretions of those infected. On this point we have some interesting information. The first division of the 7th Army Corps had during its stay in Jacksonville water carriage for its fecal matter. Each company was

supplied with a galvanized iron trough, the lower end of which was connected with the sewer. The connection between the trough and sewer was closed by a cylindrical plug, which could be raised whenever it was desired to discharged the contents of the trough. The other end of the trough was connected with a water hydrant. The trough was partially filled with water, and in this condition received the excrement. The contents of the trough were discharged at will.

The second division of the same army corps was furnished with tubs or half-barrels. The fecal matter and urine were received in these without the addition of lime, dirt, or anything else. When these tubs were filled they were carted away by scavengers, emptied, cleaned, and returned. The fecal matter in the tubs was always exposed to flies; the contents were often spilled about the camp and slopped out along the road.

The third division disposed of its fecal matter in pits, as is ordinarily done in camps. Orders were issued that the contents of the pits should be covered once, twice, or three times a day, differing in different regiments. In some regiments attempts were made to compel each individual to cover his stool as soon as deposited. It will thus be seen that in the three divisions there were three distinct methods of disposing of fecal matter. The men in these companies were supplied with the same water, the same rations, lived in the same kind of tents, in the same climate, and, in fact, the only difference was in the method of disposing of the fecal matter. In August and September there were more cases of typhoid fever in one regiment of the second division than in all the six regiments then constituting the first division, while the third division furnished an intermediate number. It will thus be seen that when the feces were swept out of camp with a minimum possibility of contamination, typhoid fever was less prevalent.

The most potent factor in the spread of typhoid fever at most of the camps was camp pollution with infected fecal matter. This was true at both the small and large encampments. It was equally true of the smaller camps, usually of one regiment, in the Northern States, and the large encampments of one or more corps in the South. The 15th Minnesota at St. Paul and Fort Snelling, the 35th Michigan at Island Lake, and the 203d New York at Camp Black became quite as badly infected as did any of the regiments at Chickamauga, Jacksonville, or Camp Alger.

The epidemic of typhoid fever was not due to sending Northern men to Southern camps, nor was it due to the massing of many regiments together, but it was due to camp pollution. In most of the camps fecal matter was deposited in pits. Flies swarmed over the infected fecal matter and then walked over the food at the mess tents. In many of the regimental camps fecal matter was deposited about the camp on the ground. There were pieces of woodland at Chickamauga Park through which one could not walk without soiling his shoes with fecal matter. In some of the regimental camps at Tampa the sinks were overflowed by the rains and fecal matter floated through the companies' streets. In many regiments paper soiled with fecal matter was blown about through the camp. In a few instances it happened that when a regiment was compelled to occupy a site vacated by another regiment, that in digging sinks for the newly-arrived command the men found themselves in the filled sinks of the regiment that first occupied the ground. In at least one company of one of the New York regiments a small cesspool was dug near each tent, and this received the washwater and probably at night the urine. In one of the Pennsylvania regiments the men of one company dug a shallow well in a location where the water was in all probability contaminated, and this company had an unusually large number of cases of typhoid fever. At Chickamauga a soldier was found attempting to run the guard by getting into one of the barrels on the wagon on its way to the spring to bring drinking water for the regiment. We walked through the regimental camp to which this soldier belonged, and we can testify to the fact that, although we picked our way, the soles of our shoes were soiled with fecal matter before we finished the round of inspection. In this way men carried fecal matter into their tents, and clothing, blankets and tentage undoubtedly became infected in many instances. These are some of the ways in which the infection of typhoid fever was spread.

We are convinced from our observations that, when water-carriage for the disposition of fecal matter cannot be secured, the complete sterilization of all fecal matter is necessary to prevent the spread of typhoid fever in camps occupied for three weeks or longer. For this purpose we have recommended that each company be furnished with a specially constructed galvanized iron trough. This trough is partially filled with a special solution of milk of lime, and is emptied

daily by means of an odorless excavator. In large camps one odorless excavator will serve a brigade, and the cost of each trough will not be more than $15. It must be evident to all by this time that the prevention of disease is the most important duty of army medical officers. We think that it is cheaper and more humane to prevent sickness than it is to care for the sick. Moreover, prevention of sickness conserves the fighting force, keeps the men in good spirits, renders good discipline more easy, prevents that demoralization that comes with every epidemic, and in every way renders an army more efficient. The success of many a campaign depends as much upon the hygienic measures adopted as it does upon the military skill of the line officers. The medical officer needs special training and should be selected with more care than has been done in the past. He should be given more authority, and then more should be expected of him.

To what extent did typhoid fever prevail among the troops encamped in this country during the summer of 1898? Owing to the aversion shown by medical officers to diagnosing this disease correctly, as has already been mentioned, it is difficult to answer this question exactly.

The following figures show the extent to which typhoid fever prevailed among twelve regiments belonging to the 1st and 3d army corps:

Name.	Time.	No. of recognized cases.	No. of possible cases.	No. of deaths among completed cases.	Total deaths.
12th New York . .	May to November,	157	490	10	17
1st Arkansas . .	May to September 15,	81	228	13	22
8th New York . .	May to September 9.	190	425	16	21
2d Missouri . . .	May to November,	180	268	17	13
2d Ohio	May to October,	184	403	14	14
1st New Hampshire	May to September 12,	211	297	7	29
52d Iowa	May to September,	175	345	20	35
1st Missouri . . .	May to September 8,	45	216	5	17
5th Missouri . . .	May to October,	47	212	8	16
31st Michigan . .	May to October,	84	239	7	9
2d Kentucky . .	May to September 15,	89	286	14	27
9th New York . .	May to September 12,	141	328	21	41
Total		1584	3732	152	261

Some explanation of this table may be desirable. The first column gives the name of the regiment; the second column indicates the period of time covered by the reports from which the data are taken. Some of the regiments were mustered out early in September, while others continued in service throughout November, and even later. The third column gives the number of recognized typhoid cases in each regiment; the fourth column gives the number of cases of typhoid fever in each regiment, according to our estimate after going over the regimental and hospital reports. The fifth column gives the number of deaths among the completed cases; the sixth column gives the total number of deaths in the regiment as reported to the War Department up to December 2, 1898. It will be seen from this table that 12 regiments furnished 3732 possible cases of typhoid fever, and we are quite thoroughly convinced that in this list of possible cases there are very few, if any, doubtful ones. This gives an average of a little more than 300 cases per regiment. In this list the smallest number of cases are furnished by the 5th Missouri, which had 212, and the largest number by the 12th New York, which had 490.

We have tried to find the mortality among the typhoid fever cases, but at present we are not able to give any exact figures. The fifth column in the above table shows the number of deaths among the completed cases of typhoid fever. It must be understood that many of these deaths occurred among so-called malarial cases. This column foots up 152 deaths among the completed cases in the 12 regiments. There were 3732 possible cases in these regiments. This gives a mortality of a little more than 4 per cent. It must be understood, however, that this is altogether too low, because there is in this computation no data concerning the deaths among the incomplete cases. We have attempted to get the total number of deaths from the records in the War Department, and the sixth column gives us figures for the total number of deaths up to December 2, 1898. These figures indicate the total number of deaths from all causes. That these figures are too low is shown by referring to the record of the 2d Missouri, in the above table. According to the figures furnished to us by the War Department, there was, up to December 2, 1898, a total of 13 deaths in this regiment, but the regimental and hospital records show us that up to November, 1898, there were 17 deaths among the possible typhoid fevers only. Supposing that the deaths reported to us

from the War Department were all due to typhoid fever, we would then have among the possible cases of typhoid fever a death-rate of a little less than 7 per cent. All that we can say then, at present, is that the death-rate among the possible typhoid cases at Chickamauga, as shown by these 12 regiments, was somewhere between 4 and 7 per cent., with the probabilities very much in favor of it being much nearer 7 than 4 per cent. Our general impression during our inspection of the regiments and hospitals was that the death-rate among the typhoid fevers was very low, but 7 per cent., or 6 per cent., or even 5 per cent., is not a low mortality for typhoid fever among soldiers. In civil practice we have a right now to expect a death-rate of not more than 7 per cent. This death-rate should be much less among men who are picked on account of their physical perfection. We will endeavor to get more exact data concerning the mortality.

It is a striking fact that the majority of the men who had typhoid fever had no preceding disease. We went into this work with the preconceived idea that diarrhœa and other intestinal disorders rendered men more susceptible to typhoid fever, and therefore, we fully expected to find that typhoid fever prevailed more largely among those who had some form of intestinal trouble. Our studies have shown us that this is not true, and that more than 80 per cent. of the typhoid fever cases do not appear upon the sick reports until they are taken with typhoid fever.

As illustrating the relation between preceding intestinal disorders and typhoid fever we will take the following from our history of typhoid fever in the 1st West Virginia. There were 260 cases of probable typhoid fever in this regiment. Five of these had the date of their illness in November, and 4 others did not belong to any company. Deducting thus, the 12 companies furnished 251 cases of typhoid fever. Supposing that each company had its full quota of 106 enlisted men and 3 commissioned officers, then 1308 men furnished 251 cases of typhoid fever; 585 individuals in this regiment are reported as having had some intestinal disorder, and apparently 723 escaped diseases of this kind. The 585 persons furnished 82 cases of tpphoid fever—1 to 7.13; the 723 individuals furnished 169 cases of typhoid fever—1 to 4.6. However, these figures do not represent the facts. Of the 82 cases of typhoid fever, 42 were not preceded by any intestinal disorder. Therefore, 543 persons who had intes-

tinal disorders of some kind furnished 40 cases of typhoid fever—1 to 13.7; and 765 persons, who had no intestinal dtsorders, furnished 211 cases of typhoid fever—1 to 3.64. A little more than 84 per cent. of the typhoid fevers in this regiment were not preceded by any intestinal disorder. It seems to us that only one conclusion can be drawn from these facts. Many of the diarrhœas must have been due to, or at least accompanied by, typhoidal infection.

Another interesting thing about the typhoid-fever cases is that in a considerable number of those preceded by some disorder, whether malaria, diarrhœa, or indigestion, the disorder occurred in such close connection with the typhoid fever as to cause us to believe that it was due to the typhoid infection. The following cases taken from the records of the 6th Ohio illustrate this point. It should be stated that in this regiment all the cases of typhoid fever, with two exceptions, were diagnosed as malaria or indigestion.

No. 1. Indigestion, August 24th to 25th; malaria, August 31st to October 8th.

No. 2. Diarrhœa, August 16th to 17th; malaria, September 20th to October 8th.

No. 3. Indigestion, September 11th to 13th; malaria, September 24th; died October 8th.

No. 4. Diarrhœa, September 5th to 6th; malaria, September 10th; still sick October 31st.

No. 5. Indigestion, September 4th to 8th; indigestion, September 15th to 16th; malaria, September 20th; still sick October 31st.

No. 6. Diarrhœa, August 14th to 15th; malaria, August 18th to October 19th.

No. 7. Continued fever, September 7th to 9th; malaria, September 10th to 11th; continued fever, September 26th; still sick October 31st.

No. 8. Continued fever, August 12th to 16th; malaria, August 19th to Septembe 21st.

No. 9. Diarrhœa, August 22d to 23d; malaria, August 25th to October 25th.

No. 10. Diarrhœa, August 13th to 16th; malaria, August 18th; still sick October 31st.

No. 11. Indigestion, September 15th to 16th; continued fever, September 24th; still sick October 31st.

No. 12. Diarrhœa, August 12th to 13th; malaria, August 19th to September 21st.

No. 13. Indigestion, August 5th to 6th; malaria, August 18th to October 28th.

No. 14. Diarrhœa, September 12th to 14th; indigestion, October 14th to 16th; continued fever, October 18th; still sick October 31st.

No. 15. Indigestion, August 16th to 17th; malaria, August 17th to September 23d.

No. 16. Diarrhœa, August 14th to 16th; malaria, August 18th to September 21st.

No. 17. Diarrhœa, September 6th to 7th; malaria, September 12th; died September 22d.

No. 18. Indigestion, August 22d to 27th; malaria, August 29th; still sick October 31st.

No. 19. Diarrhœa, September 2d to 3d; malaria, September 5th; still sick October 31st.

No. 20. Remittent malaria, September 6th to 8th; continued fever, September 10th; still sick October 31st.

No. 21. Indigestion, September 9th to 11th; malaria, September 14th; still sick October 31st.

No. 22. Diarrhœa, September 14th to 16th; continued fever, September 19th; still sick October 31st.

No. 23. Diarrhœa, August 20th to 21st; malaria, August 29th to September 1st; malaria, September 2d to 3d; malaria, September 5th to 6th; continued fever, September 29th; still sick October 31st.

No. 24. Diarrhœa, September 21st to 22d; indigestion, September 30th to October 3d; continued fever, October 6th; still sick October 31st.

No. 25. Diarrhœa, August 8th to 9th; diarrhœa, August 13th to 14th; malaria, August 20th to October 31st.

No. 26. Indigestion, August 19th to 21st; continued fever, August 29th to October 24th.

No. 27. Diarrhœa, August 4th to 5th; diarrhœa, August 7th to 8th; malaria, August 19th; still sick October 31st.

No. 28. Diarrhœa, September 12th to 14th; malaria, September 15th to 17th; continued fever, September 19th; still sick October 31st.

No. 29. Indigestion, September 15th to 16th; continued fever, September 25th; still sick October 31st.

No. 30. Simple fever, July 14th to 22d; diarrhœa, August 2d to 3d; continued fever, October 21st; still sick October 31st.

No. 31. Malaria, August 13th to 14th; malaria, August 19th to September 21st.

No. 32. Indigestion, August 21st to 22d; malaria, August 29th; still sick October 31st.

No. 33. Simple fever, August 9th to 21st; malaria, August 26th to September 30th.

No. 34. Diarrhœa, August 21st to 22d; continued fever, August to September 24th.

No. 35. Diarrhœa, August 13th to 14th; malaria, August 29th to September 25th.

No. 36. Diarrhœa, August 14th to 15th; diarrhœa, August 17th to 18th; malaria, August 29th; still sick October 31st.

No. 37. Simple fever, August 12th to 15th; diarrhœa, August 20th to 24th; malaria, August 29th; still sick October 31st.

No. 38. Malaria, September 10th to 11th; indigestion, September 14th to 16th; malaria, September 16th; still sick October 31st.

Hundreds of cases of this kind are recorded on the sick reports. In our opinion the preceding illnesses in many of these cases were connected with the typhoid-fever infection. The most rational explanation, so far as we can see, is that in the majority of these cases the infection was a mixed one, in which saprophytic germs greatly predominated in numbers. The preceding temporary illnesses were believed to have been due to the effect of the saprophytic microörganisms.

In our studies we have had frequent occasion to observe that among soldiers typhoid fever was often far advanced before it was recognized. That this was a potent factor in the spread of the disease in camps must be evident. With many unrecognized cases of typhoid fever defecating in the pits and on the ground over which men walked, drinking from the same water receptacle, eating from the same mess, and occupying tents in common with others, the chances of the transmission of the specific infection was great.

In military practice typhoid fever is often apparently an intermittent disease. The following cases illustrate this:

No. 1. Intermittent malaria, August 10th to 15th; diarrhœa, August 19th to 21st; remittent malaria, August 21st to 25th; convalescing from typhoid fever, September 9th.

No. 2. Diarrhœa, July 30th to August 5th; intermittent malaria, August 17th to 22d; remittent malaria, August 22d; granted sick leave August 27th; sent to Presbyterian Hospital in New York City, September 9th with typhoid fever.

No. 3. Intermittent malaria, August 13th to 18th; remittent malaria, August 18th; granted sick leave, August 31st; sent to St Luke's Hospital in New York City, September 9th with typhoid fever.

No. 4. Intermittent malaria, August 13th to 18th; remittent malaria, August 18th to 23d; granted sick leave, August 29th; sent to St. Luke's Hospital with typhoid fever September 9th.

No. 5. Diarrhœa, July 10th to 11th; diarrhœa, July 22d to 25th; diarrhœa, July 30th to August 4th; intermittent malaria, August 6th to 20th; remittent malaria, August 23d to 24th; granted sick leave, August 27th; sent to Mount Sinai Hospital, September 9th convalescing from typhoid fever.

Hundreds of other cases might be given to illustrate the apparently intermittent character of many cases of typhoid fever. We have stated that these are "apparently" intermittent. We do not intend to state that these apparent intermissions were afebrile. It is probable that a temperature-record would have shown that this was not the case. We mean that there were periods when the patient felt better, and for this reason was returned to duty.

The influence of change in location of camps upon the continuance of typhoid fever is exceedingly interesting. We have not investigated this subject as thoroughly as we hope to do. At present, however, I think that we can give the following conclusions:

(*a*) A regiment thoroughly infected with typhoid fever does not lose the disease when it changes its locality, even when it goes to a perfectly unobjectionable site and leaves all its sick behind. Evidence of this is shown in the history of the whole of the Second Division of the 1st Army Corps when it moved from Chickamauga to Knoxville. At Chickamauga Park this division became thoroughly saturated with typhoid fever. After reaching Knoxville, and notwithstanding the fact that the camp site was probably as fine as any in the world, the water supply unobjectionable, the nature of the soil suitable to the digging of sinks, surface-drainage good—notwithstanding all of these advantages, typhoid fever prevailed more largely than it did at Chickamauga. It is altogether probable that the clothing, blankets and

tentage of the men became thoroughly infected with the typhoid bacilli. When a regiment becomes saturated with typhoid fever change in location alone is not sufficient to get rid of the disease. We believe that it will be necessary in such a case to thoroughly disinfect clothing, blankets, tentage, etc.

(*b*) If a regiment be moved before the infection has become marked, typhoid fever may disappear, or at least decrease.

(*c*) Apparently a sea voyage of some days or weeks might rid a command not widely infected with typhoid fever of the disease. We have some illustrations of this in the troops that went to Cuba. For instance, about half of the first volunteer cavalry went to Cuba, while the other half remained at Tampa. Before the departure for Cuba, and while the regiment was altogether, typhoid fever appeared and its prvalence was confined to those companies that went to Cuba. Apparently this part of the regiment lost its typhoid fever on its way to Cuba, while the part that remained behind became badly infected.

(*d*) A regiment thoroughly infected with typhoid fever does not lose the disease or lessen the number of cases after a short voyage at sea. This was illustrated by the 19th Infantry which, after becoming throughly infected with typhoid fever, was transported to Porto Rico. The progress of the disease apparently was not in the least retarded by this voyage.

DISCUSSION.

DR. STERNBERG: I came to hear this paper because, of course, it is of the greatest interest to me, the investigation being one that I encouraged, and which I hope will have very fruitful results. It is certainly discouraging that after the lessons of the Civil War we should have had a repetition of camp infection by a disease that we recognize as a filth disease. Dr. Vaughan has pointed out the principal reasons for this. I had hoped for better things; that the profession in general was educated up to such a point that the majority of the regimental surgeons would fully appreciate the dangers; and, moreover, on April 25, 1898, I issued a sanitary circular, which was distributed everywhere, and which pointed out the danger and the means of avoiding it. But, of course, it is a great deal easier to preach than to practice, especially in such conditions as we had to contend with in our large camps of raw troops, many of them reckless men. The line officers were, many of them, inclined to consider all the talk about cleaning the camp, about flies carrying infection, etc., as a fad of the doctors, and they did not recognize the danger until an epidemic occurred. It is not so long ago that in our large cities, where there are few real malarial cases, a large number of cases were put down as such, and I have in my records reports of cases of remittent fever occurring in New York harbor and from the northern frontier where there is no such thing as malaria. We all know that in many parts of the country the same disease is reported either as typhoid fever, typho-malarial fever, or malarial fever. Here are cases, then, being treated as malarial while they are scattering the typhoid infection all over the camp, and taking large doses of quinine daily.

Dr. Vaughan and I were on a committee of the American Public Health Association, which made its report fifteen years ago, insisting upon the necessity of destroying the possibility of infection by sterilizing the excreta of typhoid patients. Our report had wide-spread distribution, but it seems that it had not the desired effect. I am led to ask myself whether the doctors throughout the country follow such a plan, and I am afraid they do not. Now these are the doctors who became our regimental surgeons. They were appointed by the Governors of the States, and became responsible for the sanitary conditions of the camps. The results have been most unfortunate. I shall not dwell upon it any further; but I will say that if it had not been for this general prevalence of typhoid fever in our camps everywhere, Camp Black, in New York State, the camp in Minnesota, where the regiment never left its home camp, the camp in Honolulu, and elsewhere, the work of the medical department would have been comparatively easy, for aside from that the health of our troops has been good, except those who, at Santiago, were exposed to very unfavorable conditions.

The question has been brought before you very forcibly by this paper, and all I can add in closing is the expression of hope that the results of this war

may be impressed upon the profession, and that there may be some way of avoiding similar disasters in the future, especially as we are assuming the rôle of a great nation that proposes to take control of large cities like Havana and show the world how to clean them up. I consider it very humiliating that we should have had such a failure during the last war.

DR. PEABODY: It seems to me this paper of Dr. Vaughan's constitutes the most terrible indictment I have yet heard of the general efficiency of the army surgeon. The daily papers have been full of general charges, but these specific charges of ignorance constitute really the most frightful indictment yet brought to our notice. It does not seem to me that such a paper should be allowed to pass without comment, and I suggest that it is quite in line with progress that this paper should be printed and used as a tract, and that every man in the army medical department now and those to come in should be required to pass an examination upon it.

As to the possibility of disinfection of typhoid stools, we come there upon a very difficult problem. I am perfectly sure myself that the methods commonly employed are wholly inefficient. The passing of the stool into a bedpan containing 1 to 1000 bichloride or 1 to 20 carbolic solution does not constitute disinfection of it, and yet that is the most that is usually done. It has been shown that it is necessary to stir the disinfectant with the stools, and to allow them to remain in contact with it for twenty-four hours in order to get sure results. As we know, many cases of typhoid have constipation, and so far as I know there is no method of disinfecting a formed stool short of actual combustion.

DR. STERNBERG: In reference to the medical department of the army, I wish the gentlemen to remember that it was inadequate even to the small army in peace times (25,000), and I had urged an increase. When the war broke out some of our men were ill, and after the campaign at Santiago we had twenty-five or more disabled. The medical department previous to the war had but few officers, but they were well trained, and while they are not all ready to make diagnoses without mistakes, they are well equipped. The majority of the officers at Montauk were acting assisting surgeons who had had no previous military training.

DR. DOCK: I brought with me some temperature curves taken in the camps, and want to say a few words about the practical diagnosis of typhoid as encountered in the army. It is not necessary for me to defend the army medical service, for what struck me at the camps was the evidence of lack of knowledge of typhoid and malarial fevers in the profession at large. I came into contact with probably from sixty to seventy-five young physicians of a very good class, such as we would take into our hospitals as internes. Most of them, however, had no hospital experience, and very few seemed to have had any clinical experience with typhoid. Almost all the surgeons who went into the service seemed to have the idea that when they went to the

camps they would find large numbers of cases of malaria, and some went with large private stores of quinine. One regimental surgeon told me he advised all his men to take 200 grains of quinine and a bottle of paregoric each, and instructed them to use it on the first appearance of disease.

At the Sternberg Hospital there were some five hundred cases of illness when I arrived, and it is safe to say that four hundred of them were typhoid fever, although but very few of them had that diagnosis made at the time, and practically all were taking quinine. Some were taking small doses, as in the case from whom this chart was taken, 1 to 3 grains three times a day, together with 3 grains of salol; what the latter was given for I do not know. Some took very large doses of quinine. Among these cases there was a great deal of diversity in the clinical pictures, although in most a diagnosis could be made with little difficulty.

Here is a chart showing the later stages of a case in which the nurse said the previous course had been rather intermittent. Many of the cases had chills in the beginning and a rather intermittent fever; others had a continued fever, as in these other charts. Many of both kinds were given quinine, from 40 to 70 grains a day. It was somewhat curious to see how this dose was arrived at. One doctor's usual order was 10 grains every six hours, and in answer to my question how he hit upon that dose, he said it was "Osler's dose." When I begged him to show me his authority he brought me Osler's book and read that patients suspected as malarial were to be given 20 grains a day, "but as our patients get their medicine at night as well as day, they get 40 grains." Here is a chart of a moderately severe typhoid fever treated with quinine, 10 grains every six hours, and it will be seen that the temperature dropped about one degree after the patient was first admitted—a fact that we are all familiar with in cases treated in various ways; but afterward it kept on uninfluenced by the quinine, though I was assured by the doctors in many such cases that they could "see the effects of the quinine on the patients." The effect does not show on the chart. Here is another chart from a patient who took 40 grains a day for awhile, and then 20 grains, and finally was put upon a proprietary preparation, antipyretic, also without notable effect.

These charts were prepared in the face of many obstacles, and I give simply a few of the characteristic ones to give material evidences of the way the cases were treated. I could just as easily have taken forty charts as two if I had time.

These doctors were unable to carry out scientific tests, of course, because they had no microscopes and no supplies for Widal tests. About the time I reached the Sternberg Hospital, Dr. Craig had begun making Widal tests, and in about three hundred cases tested secured a positive reaction. The examinations of the blood for evidences of malaria were made under many difficulties on account of the enormous doses of quinine given. It was useless to draw conclusions from negative examinations while under its influence. I had frequent examples of the comparative ease with which real

malarial cases were stopped under the influence of quinine, and I have here a chart that shows it. Curiously enough, this chart came from a patient whose condition was diagnosed as typhoid. It is quite true he looked like a typhoid patient, but the blood examination showed a double tertian malaria, and the Widal test was negative. He had been given 18 grains of quinine at two doses before I examined him; no more was given, and he had no more fever. I frequently examined men who gave the history of having one or two chills, and though the blood was negative, possibly these cases were malaria, but the examinations showed the ease with which the fever stopped as compared with the protracted cases—the cases that formed the large majority of camp diseases of a serious kind. I think we can assume, therefore, that most cases were not malarial, and probably not even associated with malaria.

The misunderstanding regarding the symptoms of typhoid and the exaggerated belief concerning the effect of quinine in malarial fevers was a striking feature of the volunteer medical service.

I will pass around a chart of some interest, for it does not often happen that we see a typhoid chart in the first week. The patient was taking his temperature for several weeks because of a suspected malaria. He suddenly had a chill, and I saw him shortly afterward, but not having my microscope at hand I begged him not to take any quinine. The next day he had another chill, lasting about an hour, which appeared characteristic of malaria, but a blood examination showed no malarial organisms. On the third day he had another chill, followed by fever and sweating, which was not, however, very heavy. The temperature, so far from being like that of intermittent fever, was a slowly ascending fever, and the third was the last chill. He had an irregular typhoid, which lasted about six weeks. In that case the appearance of the chills, notwithstanding the fact that the man had no malaria, is interesting in connection with the symptomatology of the early stage of typhoid fever.

Many things might be said of the practical work in the army, but I will mention only the matter of temperature taking. I probably had better opportunities of seeing some of the details of the work than others, because I was not in uniform, and many of the nurses and doctors had no idea that I was a doctor. I frequently had occasion to see that the soldiers had learned how to be discharged ahead of time or to be allowed to enter town. They simply held the thermometer between their teeth and breathed upon it. They would ask each other "Did you get off?" "Oh, yes, I fooled the old man; it only went to 97°." These men would then go to town and probably eat two dinners and return with a relapse. I doubt if this could happen with an experienced army surgeon.

DR. JACOBI: The lamentable ignorance of so many of the medical officers is an established fact and accepted by all. In connection with that I had a painful surprise in what Dr. Sternberg had to say. It appears from his

remarks (at least I concluded so) that he had no hand in the selection of these officers—that they were not selections of his, but were appointed by the Governors of the States.

DR. STERNBERG: All the regimental officers were appointed by the Governors.

DR. JACOBI: I do not know what the rights or duties of the Surgeon-General are, but it should certainly not be his duty to accept all the rubbish that may be sent him by an ignorant Governor. If he is compelled to accept the appointment of these so-called medical officers it is about time that the practice should be abolished in the interest of the service.

DR. STERNBERG: Under the laws of the country the regiments of the States had their officers, line and medical, appointed by the Governors. By my recommendation a board was appointed in each State to examine these officers. The Governor appointed two members of that board, and, where practicable, we detailed one medical officer for the board. I do not want to be understood as saying that these men who went out with the regiments were worse than the men who stayed at home. They were, many of them, good physicians and surgeons, and I think up to the average of the profession of the part of the country they came from; not the best men, because men with large practices do not offer themselves for such places. The trouble is that even had we selected the men they would still have much to learn about camp sanitation, and I believe that one of the troubles is that the medical schools do not give sufficient attention to this matter, and the profession in general is not so thoroughly informed on matters clearly sanitary as they should be. Many of these men afterward became very competent medical officers and went home with their regiments in good condition, but it took time to prepare them, and it was at the expense of the soldiers.

DR. S. SOLIS-COHEN: There are some points in the paper and discussion which I think ought to be emphasized. In the first place, I want to say a word for the volunteer regimental surgeon. I may not use the exact military title, and I am drawing no distinction between physician and surgeon—I mean the medical officer from civil life. Do not make him a scapegoat, but place the fault where it belongs, with the line officers. It is a matter of record that Col. J. Biddle Porter's regiment, the Second Pennsylvania, had no typhoid fever and but two cases of illness from any cause. This was due not only to the efficiency of the volunteer surgeons, Drs. Burgin and F. A. Packard, of Philadelphia, but also to the great efficiency of the line officers. The colonel of the regiment and his subordinate officers thoroughly carried out the sanitary measures suggested by the surgeons. On the other hand, Dr. Sternberg has stated here to-day that in many, perhaps most, regiments the line officers thought that the sanitary suggestions of the surgeons were

simply "a doctor's fad" and neglected them. We have Dr. Senn's testimony that his advice was ignored, just as the Surgeon-General suggests took place generally. This is the most important contribution made to the whole discussion in so far as it tends toward fixing the responsibility; and it shows this awful weight is not upon the medical profession, but upon the military authorities. Certainly, whatever the shortcomings of the medical officers, they are not to blame to anything like the extent that the paper, and the Surgeon General's other remarks if unqualified, might seem to laymen to imply. It must be remembered that the medical officer had no executive authority, and if the colonels and captains refused or neglected to issue or enforce the orders concerning sanitation that he had suggested, the blame must be theirs, not his.

Regarding the diagnosis of malaria and typhoid fever, I happened to be on duty at the Jefferson Medical College Hospital last summer when we had the men from Tampa, Fernandina, and Porto Rico. Among these soldiers were unquestionably cases of simple malaria and cases in which both diseases coexisted. This was shown not merely by ordinary clinical phenomena, but by finding the organism of malaria and by the positive reaction to Widal's test. Dr. Da Costa at the Pennsylvania Hospital, Dr. Anders at the Medico-Chirurgical Hospital, Dr. Daland at the Polyclinic Hospital, and I think Dr. Wilson at the German Hospital have reported cases of the same kind observed in Philadelphia; and if these were found in the hospitals I see no reason to deny that both simple malaria and mixed infections could have occurred in the camps. However, I believe it would be a good rule in camps to reverse the maxim of the law, "Hold every man innocent until proved guilty," and hold every case of fever or of diarrhœa to be typhoid until it is proved to be something else. Then all precautions against infection would be taken from the first.

Without undertaking to defend the diagnosis of malaria, criticised in the paper, I should like to ask Drs. Vaughan and Dock, or the Surgeon-General, or any one who can answer, whether in these cases of malaria, which were not malaria, but typhoid, there had been the clinical symptoms of chill, sweat, intermission or remission, and periodicity? It is hardly a common experience for cases of unmixed typhoid to begin or continue in such manner. It is certainly rare for large numbers to do so contemporaneously. The presence in such cases of a common complicating factor is suggested. With such a history the failure to find organisms after prolonged large doses of quinine would not exclude malarial beginning; nor would the subsequent development of typhoid exclude malarial beginning, considering our present knowledge as to mixed infections.

A suggestion I should like to make is derived from my personal experience, and that is the early administration of the double hydrochlorate of quinine and urea in cases suspected of malaria, not merely for its therapeutic effect, but for its diagnostic value when the microscope is not available. I presume other salts of quinine administered hypodermically might be equally useful, but I find this the easiest to give in that manner. In such cases of malaria

as are found north of Mason and Dixon's line and east of the Ohio River the paroxysms are usually checked either six and one-half days or for thirteen days by a single injection of 15 grains; and I should think any case that failed to yield to two such injections to be almost certainly other than malaria.

DR. KINNICUTT: It seems to me that Dr. Vaughan has shown in a striking way the probable cause of the prevalence of typhoid in the late war, and unless medical officers have either sufficient knowledge or power to enforce proper sanitary precautions in the army I do not see how we can hope for anything better in the future. I had the opportunity of inspecting the sanitary conditions at Camp Montauk, and there, although regular army officers were in charge, the methods of dealing with sanitary problems seemed to me very insufficient. I believe that a large number of cases of typhoid arose in camp that were never reported as having their origin there. I judge this from the fact that we received into the New York hospitals a number of men who had never been in the regimental or general hospitals, but who, getting a temporary leave of absence, were found, on reaching Long Island City or New York, to have typhoid of the second or third week. We received into my wards in the Presbyterian Hospital cases as late as the middle of September of men who had been in the camp continuously for two months.

The disinfection of the excretions from typhoid fever cases was exceedingly inefficient. While in some camps the methods of disinfection were better than in others, they were deficient everywhere; and when we remember that not only the stools of typhoid patients, but the urine, even after convalescence is established, contain the specific bacilli, the necessity for a more careful inspection of all excretions is forced upon us.

Again, the method of dealing with the bed and body linen of typhoid cases was for a long period inexcusable. Without any adequate disinfection, it was allowed to accumulate, where swarms of flies had easy access to it, until a large amount was collected, when it was carted away and burned. It should be said that the topography of the site of the Montauk camp was unfavorable in many respects for satisfactory sanitation. Stagnant pools, many of considerable size, are very numerous; in a single cavalry camp I counted ten such pools, and oftentimes it was found impossible to locate the latrines at sufficient distance from them to avoid their probable pollution. The engineers in charge of the water supply of the camp informed me that probably the majority of these pools had become specifically infected. In questioning the officer in regard to the use of water from the pools, I was told that it was strictly forbidden for any purpose, and yet I saw men take dishes from a regimental kitchen not a dozen feet distant from a pool and at a similar distance from a latrine, wash them therein, and immediately afterward place food upon them. This is the sort of thing I fancy that medical and line officers have to contend with constantly. I admit that the satisfactory sanitation of large camps is difficult, but I believe that fuller knowledge

of sanitary problems on the part of both medical and line officers, and the conference of greater power upon the former, would bring about better results.

DR. VAUGHAN: I would like to ask Dr. Cohen if he can furnish me with a history of any cases reported from Philadelphia of malaria amongst the soldiers coming from Fernandina or any other camp in this country. As I stated in my paper, there undoubtedly were a few cases of malaria among the soldiers who remained in the United States, but so far we have been able to find only a few cases in which the diagnosis was confirmed by blood examination.

I think, from the remarks that have been made in this discussion, that my statements concerning the regimental surgeons were more critical than I intended that they should be. It is my belief that the average regimental surgeon among the volunteers was better than the average doctor, taking the country throughout. Of course, these surgeons were appointed by the Governors of the States, and there were many incompetent men. Several regiments were under the charge of irregular practitioners. I desire to emphasize the fact that the medical officer is often powerless to prevent the camp pollution which was the cause of so much typhoid fever. It is to be greatly regretted that our line officers have no education in sanitary matters. Hygiene is not taught, I believe, either at West Point or at Fort Leavenworth. This is not as it should be.

ANOMALOUS ERUPTIONS IN TYPHOID FEVER.

By J. M. Da COSTA, M.D., LL.D.,
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The characteristic lenticular eruption in typhoid fever has been so well studied that there is little to be added to our knowledge of it; but, irrespective of the significant rose-spots, there are rashes which are comparatively rare, imperfectly understood, and become the cause of confusion and error. The two that I shall specially examine are a diffused erythema simulating scarlet fever and an eruption like that of measles. Let me take up the scarlatiniform eruption first and illustrate it by a few cases.

Case I.—Sarah V. (No. 2647), aged fourteen years, was admitted into the Pennsylvania Hospital on February 11, 1898. She was in the seventh day of typhoid fever; the temperature was 103.2°, the Widal reaction was positive. From the first the mottled look of the skin attracted attention; the characteristic rose-colored spots of typhoid soon became unusually profuse; they were seen on the abdomen, back, chest, and even on the face. The case did not prove a severe one. A remarkable feature was the appearance on the night of the twelfth day of the disease of a bright red erythematous eruption, readily affected by pressure and very generally diffused, but especially marked on the face and back. There were blotches of more vivid hue than others; there was no itching. No rise in temperature or abnormal state of the urine was observed in connection with the rash; the highest temperature attained was only 100.2°. No sore-throat existed, and the symptoms did not become aggravated by the occurrence of the eruption, which passed away by morning. The case went on uninterruptedly to recovery.

A yet more striking illustration of the scarlatiniform rash, and one in which this lasted very much longer, was afforded by the next case.

Case II.—Katie F., a young woman, was admitted into the Pennsylvania Hospital on March 6, 1897, having been ill for about five days. She had

been previously in good health, and had never had either measles or scarlet fever. On admission to the hospital her temperature was noted at 103°, but it soon rose to 105°; the urine showed a trace of albumin, and one finely granular cast was found. The skin was very fair, so that any spots could have been readily detected, but none were observable. The next day there appeared on the face and arms a bright red, erythematous rash, which lessened somewhat after sponging, and was not always equally distinct, seeming to come and go, though never wholly leaving. There was no rash of the kind on the body, but it was specially observed that pressure on the skin everywhere produced a red spot which only slowly faded. The temperature ranged between 103° and 104 2°. On the 9th great disturbance of respiration was perceived, the breathing fell to twelve in the minute, and was jerky and irregular, and the erythematous rash which had disappeared showed itself again on the face and arms, giving the patient the appearance of scarlet fever—an appearance which was increased by a redness of the tonsils and the pharynx, the latter being covered with tenacious mucus. She was very ill, but the temperature was not materially different; during the night it ranged from 103 2° to 104.6°, and she was very delirious.

On the 11th the rash was still visible, and still could be made to disappear temporarily on pressure. It was again noted that none was to be seen on the body, though it now showed itself on the back of both legs; around the elbow-joints it was much less marked than on the back of the hands and forearm. Few of the characteristic lenticular typhoid spots were discernible; there were two doubtful ones on the chest. The Widal test gave a positive reaction. The influence of cold sponging was very irregular. At one sponging the temperature fell as much as six degrees; at another, of similar length and thoroughness, but four-fifths of a degree. As the case advanced the urine contained rather more albumin, and red corpuscles and quantities of hyaline and pale granular yellow casts were found. The patient died six days after admission into the hospital, near the end of the second week of typhoid fever, the rash being evident to the last. At the autopsy a great number of prominent and swollen solitary glands and Peyer's patches were seen, but none were ulcerated. The spleen was large and soft and weighed ten ounces. The lower surface was slightly mottled; the posterior portions of the lungs were congested; the kidneys were large, weighed seven and a half ounces; the substance was firm, the capsules adherent. The rash was not discernible on the surface of the body.

There are in this case some points for special study. First, the scarlatinal rash appearing in the first week and at a time in advance of the characteristic rose-spots. The rash was uniform, was not, as in the first case, preceded by mottling, was easily influenced by pressure, did not apparently modify the temperature, and persisted to the last. In its early appearance it was like a case described by Murchi-

son,[1] in which a delicate scarlet rash all over the body preceded for two or three days the lenticular spots of enteric fever. The scarlatiniform rash may remain through the fever, though it rarely does so. Irrespective of its appearance in the first week, it may come on late in the disease, and I have known it to manifest itself even in convalescence (case of Thomas G., Pennsylvania Hospital, December, 1880) and to return in a relapse. Its character may be thus described: It is a uniform red rash, like scarlatina; it is seen all over the body, though not so in every instance. It is more distinct in some places than in others. It is easily influenced by pressure. It has its periods of greater or less intensity, of partial disappearance, of vivid return. It lasts generally a week or somewhat longer. It passes away without desquamation—at least I have never seen this happen. It does not perceptibly influence the course of the temperature. It is for the most part unconnected with sore-throat or with albuminuria. As regards albuminuria, I have observed this in some of the cases I met with, but it was a prior condition connected with the typhoid fever. With reference to sore-throat, this was in a mild form in Case II., and Jenner mentions an instance in which slight sore-throat was an accompaniment, and typhoid fever was mistaken for scarlet fever. Save under the exceptional circumstances of attending sore-throat and desquamation, there is no difficulty in determining the two diseases, or in diagnosticating that scarlet fever is not intercurrent in typhoid.

Rarer than the scarlatiniform eruption, and much more misleading, is an eruption like measles. This case may serve as an illustration:

CASE III.—Richard G., aged twenty-eight years, was admitted on November 26, 1886, into the Pennsylvania Hospital on the eighth day of typhoid fever. The face was flushed, the temperature 103.4°; there was marked hebetude. The abdomen was tympanitic and its surface covered with a coarse, slightly papular eruption, not crescentrically arranged and not disappearing on pressure; besides, there were a few rose-colored spots. In the course of the fever the eruption faded slowly and imperfectly, and was still perceptible when convalescence was reached. It retained its coarse appearance, and never showed itself on the limbs or thorax or the face. The notes speak of its similarity to the rash of typhus. There were also numerous sudamina. The temperature at one time reached 105°. The urine was free from albumin, though once a trace of albumin and a few hyaline casts were observed.

[1] Case XLV., Treatise on Continued Fevers.

In this case the measly eruption was limited in its extent. It was much more diffused in the next case, which, moreover, afforded a good opportunity of studying the question of its association with any temperature changes.

CASE IV.—John McG., a soldier, aged nineteen years, was sent to the Pennsylvania Hospital on November 15, 1898, suffering with typhoid fever. He had been ill for two weeks, and there were many rose-spots on the chest and abdomen. The temperature was 104.6°, the face very flushed, the spleen much enlarged; the urine contained albumin as well as a few hyaline casts; the Widal test gave a positive reaction. Five days after admission an eruption closely resembling measles appeared on the chest, abdomen, back, and upper part of the thigh, and, later, more sparsely on the legs, and yet more sparsely on the arms. On the face there were not many; they showed themselves late, and were less distinctly measly in appearance; in the notes they are described as blotches. Nowhere was there a crescentic arrangement of the raised red spots, which, however, in many places coalesced, and did not disappear on pressure. They passed away in five days, without itching or desquamation, the blotches on the face first, those on the legs last. The eyes were slightly injected, but no catarrhal symptoms existed. There were many places on the chest and abdomen in which the rose-colored spots were perceptible near the measly rash. Much hebetude was observed while the rash lasted, but as hebetude had been noticed from the time the patient was first seen, it could not be associated with the occurrence of the rash.

The appearance of the rash was not combined with any marked temperature changes; on the 18th the temperature ranged around 103°. On the 19th, the day preceding the eruption, the temperature at 9.20 A.M. was 101.6°. It rose during the day to 103°, modified, however, by sponging. During the night it continued to rise, until by 9.30 A.M. of the 20th, the day the measly eruption appeared, it reached 103.8°. On that day the temperature slowly fell, except for occasional rises, which were kept in check by sponging, until by 8 P.M. it had declined to 102.6°. During the night it continued to fall, the rises still being kept in check by sponging, until by 9.10 A.M. on the morning of the 21st it had reached 101°. During the 21st it went up slowly, passing to near 102° by 9 30 P.M., and continued to rise during the night until, by the 22d. at 9.20 A.M., it had passed to 102.6°. During the 22d the line was gradually downward, with the exception of one decided rise at 4.10 P.M., when it reached 103.8°, this rise being promptly influenced by sponging. On the 23d the range of temperature was, on the whole, lower than on the 22d, the highest attained being 101 6° at 7.40 P.M., and the lowest reached being 100° On the 24th the temperature again went up, and on one occasion, at 1.40 P.M., reached 103.6°. During the night it steadily fell, and on the 25th, the day of the disappearance of the eruption, it was 98.6° in the morning, though once in the day it reached 101.8°. These details

of temperature are given that we may ascertain if the eruption exercised any influence on it. On the whole, the temperature showed only the zigzag which is common at this stage of typhoid fever, and did not appear to be influenced by the eruption. If any other inference were drawn it would be that the temperature was somewhat higher in the twenty-four hours preceding the eruption, and fell slowly on the day of its occurrence. The patient soon entered upon steady improvement, and was entirely convalescent sixteen days after the disappearance of the eruption.

The similarity of these cases of typhoid fever with measly eruption to typhus fever is very great, and, when we have cases in which the nervous symptoms are pronounced and enteric symptoms absent, it is very difficult to come to a conclusion, unless the malady has been seen and the temperature been studied from the beginning, for the measly rash common in typhus fever and very uncommon in typhoid has in both much the same appearance. How much alike typhoid with measly rash may be to typhus is proved by the following case:

CASE V.—John O'R. (No. 2457), aged eighteen years, previously in excellent health, living in good surroundings and not known to have been exposed to any disease, was admitted on December 12, 1898, into the Pennsylvania Hospital with a fever of a low type, stated to be of eight days' duration and to have begun with epistaxis and vomiting. His face was flushed, he was delirious, the tongue was dry and brown, the pulse weak, the temperature 103.6°, the spleen large; albumin and granular and hyaline casts were found in the urine; rose-spots were seen on the abdomen; the Widal test was positive. He presented altogether the picture of a case of typhoid fever, with marked prostration and cerebral symptoms. The delirium was the most striking feature, and in it he got out of bed and attempted to throw himself out of the window, but was fortunately caught. Two days after admission, and on the tenth day of the disease, he was covered from head to foot with a profuse eruption. On the face, hands, and feet it was as evident as on the rest of the body, and, though influenced, it did not disappear on pressure. It was composed of numerous spots of irregular form, very slightly elevated above the skin, and precisely like the measly eruption often seen in typhus. The similarity to this disease became now greater and greater, and was heightened by the absence of enteric symptoms and the occurrence on the left side of a true pneumonia of the base with rusty sputum—a form of pneumonia much more common in typhus than in typhoid. The eruption was so thick over the body that there was scarcely a pin-point free. It was not crescentically arranged; here and there it was petechial. Fearing that the case might, after all, be typhus, the patient was carefully isolated and then removed from the hospital, as a sorrowful experience of having had cases admitted into the Pennsylvania Hospital, some years ago, that proved to be

typhus,[1] and that resulted in our having within its walls very many serious instances of the disease before we got rid of it, determined me to let the rest of the patients and the attendants run no risk. The similarity of typhus remained great to the end. The temperature, the day after he left the hospital, fell by crises, as it often does in typhus fever; the eruption showed merely as brownish traces. Another Widal examination gave positive results, and the patient slowly recovered.

Looking back over the history, though the case is still not free from doubt, I believe it to have been one of typhoid fever, rendered uncertain chiefly on account of the peculiar measly eruption here under consideration.

Another error likely to arise is due to the occasional occurrence of true measles in typhoid fever. This intercurrence may be studied in the two cases now to be detailed.

CASE VI.—Gerano L., an Italian, aged seventeen years, was ill with typhoid fever for a week when admitted into the Pennsylvania Hospital on January 17, 1898. Diarrhœa and tympany were absent, but the typhoid eruption on the chest and abdomen showed very clearly through his dusky skin. By the 26th of the month the morning temperature was 99°, but it rose in the evening to 102° and slightly beyond. On the 27th and 28th there were the same morning remissions and evening exacerbations to between 102° and 103°. On the 29th, the morning temperature being 99.6°, the conjunctiva was noticed to be injected, photophobia was complained of, there was some cough, and an eruption of measles showed itself. The temperature rose to 102.1°, and went on rising as the eruption spread over the body, until on the 30th it reached 105°. On the 31st it dropped to 102°, and the catarrhal symptoms persisted. On February 1st the temperature became normal; the rash was fading. The boy was then transferred to the children's ward, which at that time contained a great many cases of measles, and where he convalesced.

CASE VII.—Paul B., a soldier, aged twenty-one years, admitted to the Pennsylvania Hospital on September 20, 1898, with typhoid fever. By the 26th his temperature had touched normal, he was sitting up in bed, and hungry. On the 29th the thermometer marked the normal, or, at the highest, 99°. He was noticed to have coryza, injected eyes, headache, and cough. Soon the temperature began to rise, and on October 5th it was at 101°, and an eruption of measles appeared on the face. The next day the whole body was covered with measles. On the trunk the crescentic arrangement was noticeable; severe itching was complained of. It was ascertained from the patient by Dr. James C. Wilson, under whose care he then was, that he had never had measles, but had been exposed to it thirteen days before the catar-

[1] "Researches on Typhus Fever." American Journal of the Medical Sciences, January, 1866.

rhal symptoms appeared, while riding to the hospital train in an ambulance with a case of measles. The Widal test, make while the measles existed, was negative, but there was a positive diazo reaction. The urine showed uric-acid crystals, but neither albumin nor sugar. The temperature on the second day of the eruption fell to 99°, and subsequently was subnormal. Desquamation was noted on the fifth day. The recovery was a good one, except for a double phlegmasia dolens which protracted it.

When we contrast these cases of coexisting measles and typhoid fever with cases of typhoid fever in which a measly rash happens, we find striking differences. First, in the character of the eruption. This in true measles is coarser, more markedly papular, and has the well-known crescentic arrangement, which is not seen in typhoid fever. Secondly, there is itching and there is desquamation, which are also not observed in the typhoid fever rash. Moreover, the presence of the coryza and catarrhal symptoms is very significant in the intercurrent measles. But of greatest value and meaning is the temperature record. In the measly eruption of typhoid the eruption has no marked influence on the temperature, or greater variations are not met with than belong to the stage of the typhoid fever in which the measly eruption may occur. It is different, as is seen by studying the temperature in both of the cases just described, in intercurrent measles. The temperature here rises decidedly in the days immediately preceding the eruption, in the prodromal stage, exactly as in ordinary measles, and it goes on rising, or remains high, with the spreading eruption. This is quite unlike what happens in the measly eruption in typhoid fever. Where we are nearing convalescence, and the temperature has been ranging around the normal line, these temperature changes are of greatest value in diagnosis. They are necessarily less so earlier and while the fever temperature of the enteric fever itself is still a pronounced one.

We have thus described a scarlatiniform eruption, a morbilliform eruption, and also spoken of the mottling of the skin. This mottling, as in typhus, is due to a subcuticular rash, and may remain as the only eruption, or precede or attend either of the other kinds. The interesting question now arises, Are all these really separate forms, or merely different expressions of the same pathological condition—in reality one affection? I believe they are one, for I have seen them combined in the same patient and apparently interchangeable. Here is a case in proof:

CASE VIII.—Walter R. (No. 1684), a soldier, aged twenty-two years, brought from Camp Meade, was admitted into the Pennsylvania Hospital on September 20, 1898, with typhoid fever. When a child he had measles and scarlet fever. He had also had pneumonia and a previous attack of typhoid fever. The day of admission, and as nearly as could be ascertained the seventh of the disease, the patient had a temperature going from 103.6° to 104.8°; there had been epistaxis; the bowels were very loose. The next day one or two lenticular rose-spots were observed on the abdomen, but what particularly attracted attention was a strange general mottling of the skin, especially marked on the chest, abdomen, and thighs. By the 24th the mottling was nearly gone; a few new rose-spots were observed on the left side of the abdomen. The temperature, that had been ranging between 102.5° and 104.4°, was somewhat lower—between 102° and 103.6°. On the 27th, though the mottling could still be seen, it was very indistinct, but many rose-colored typhoid spots were perceptible. On the 28th, the fifteenth day of the disease, a curious coarse, granular eruption, like measles, but not crescentically arranged, and affected by, but not disappearing on, pressure, showed itself on the shoulders and upper part of the arms. It was not associated with any rise of temperature; on the contrary, before its appearance the morning temperature marked 99°, the lowest it had attained at all, and during the evening it rose to 104°, about the same that it had been on the two previous evenings. The tongue was dry and cracked; there were no bronchial symptoms. The next day the measly rash still persisted; it was evident on the shoulders and upper part of the arm, and there was in addition most marked redness of the neck and lower part of the arms, of the hands, and of the chest, closely resembling scarlet fever. Neither coryza nor sore-throat was present. The scarlet fever redness left white traces when the fingers were rapidly drawn across the skin, but the hyperæmia returned. There was no redness of the face. The urine was acid, and contained no sugar, no albumin, or casts. The Widal test gave a positive reaction.

Four days after the appearance of the measly rash it had gone entirely, and the scarlet fever redness was only visible on the neck, and even there had faded. The general mottling of the whole body remained. On the afternoon of the same day the temperature, without any apparent cause, went up from 101° to 103°, and the erythematous scarlatiniform rash at once returned on the neck, chest, and wrists. There was no recurrence of the measly rash; the flush of the skin vanished in forty-eight hours and came back no more. Lenticular typhoid spots remained. The patient now entered upon convalescence.

The pathological conditition is, I think, a hyperæmia of the skin, with here and there in the measly form an exudation in its layers, most likely a swelling and thickening of the corium and rete Malpighii, much as it exists in measles; but I can merely surmise this, as I have no anatomical observations to offer. It is not easy to deter-

mine how these eruptions are produced, and while several views suggest themselves, no definite proof can be given of their absolute correctness. That the rashes are not caused by the administration of any remedy, which like quinine or iodide of potassium gives rise to cutaneous eruptions—a dermatitis medicamentosa—is certain, for they may be encountered no matter what the treatment employed. The bath treatment is not responsible for them. It was not used systematically in any of the cases detailed in this paper, though in some with high temperature the bath was at times resorted to.

The anomalous rashes may be the result of the irritation of the skin from the bacilli in the infected blood, but I believe rather that they are the expression of disorder of the cutaneous nerves—that they are due to the vasomotor disturbance—but how this is caused is very doubtful. It, too, may be from direct bacillar irritation, though rapid changes in the eruption, its appearance, often sudden, and disappearance, equally sudden, are against this view. More likely is it from the blood infection, but whether this be due to the toxins from the bacilli or the absorption of the broken-down material in the diseased intestine must be a mere surmise. Yet we have a strong analogy in the production of ordinary urticaria, which we constantly see arising from the absorption of products of certain articles of food that are not readily digested, but which is also met with from purely nervous causes, as from mental excitement or sudden emotion; and it is a remarkable fact that urticaria, too, sometimes happens in typhoid fever. I have myself never seen any instances, but they have been described by Griesinger, and Dr. Woodbury has recently called my attention to a case that occurred in his practice.

The nervous element and the vasomotor disturbance are certainly very strong factors in the production of these typhoid fever rashes. Lemaigre,[1] who does not believe that they are always due to the same cause, cites a case of Siredey's, in which a man went on having scarlatiniform eruptions for years afterward. The first of these rashes happened in typhoid fever, and was even followed by desquamation. He recovered entirely, but had nine subsequent attacks in the succeeding years, each also followed by desquamation.

The nervous element showed very strongly in this case, which was under my care at the Pennsylvania Hospital:

[1] Thèse de Paris, 1888, No. 209.

CASE IX.—Thomas G., aged twenty-five years, a man of excellent physique and good habits, was in the Pennsylvania Hospital with typhoid fever in September, 1880. During its course marked flushing of the face was noticed, and he stated in explanation that he always flushed readily and from the slightest cause. There were successive crops of rose-spots, even on the arms. During convalescence he had an attack of general erythema, looking like a scarlet fever eruption, but unconnected with sore-throat. He was discharged from the hospital November 22d, and returned in December with severe pain in the back and the sciatic nerve on the right side, said to have followed sleeping in a cold, damp place. It was attended with moderate fever, which lasted for nearly two weeks, and concerning which it was doubtful whether it was a typhoid fever relapse or not. It was not accompanied by rose-spots or enteric symptoms or albuminuria, but as it kept up without apparent cause it was looked upon as a typhoid-fever relapse. In its course it was observed that whenever he was spoken to in a decided manner there was flushing of the whole surface; indeed, the arms and face especially flushed under the least excitement. The flushing in the face was attended with a sense of heat, but this was not the case in the rest of the body. After keeping quiet for a few minutes the erythema always subsided, leaving a mottled appearance of the surface. There was no sore-throat, and no desquamation ever followed the erythematous flushings, but engorgement of the capillaries gave to his skin the appearance of scarlet fever. It was, however, only in parts uniform; in others in uneven patches, and it was not attended with any feeling of cold or with itching. There was never any evidence of rheumatic affection of the joints, muscles, or heart. The temperature, which ranged about 101°, did not become normal until eighteen days after his readmission into the hospital, and he was soon afterward discharged.

There is nothing in these rashes which seems to add gravity to the prognosis. It is true—though there are instances in this paper which show the contrary—that they mostly happen in severe cases of typhoid fever; especially does the morbilliform eruption, which is much more apt to occur later in the disease and to be associated with graver symptoms than the scarlatiniform rash. But the prognosis is to be determined by these symptoms rather than by the eruptions; and, as regards treatment, they call for no special line of therapeutics. As febrile albuminuria may coexist we must pay close attention to the renal secretions. It is from the point of view of diagnosis and pathology that these rashes merit attention and serious study.

REMARKS ON OTITIS MEDIA AND EARACHE IN LOBAR PNEUMONIA OF CHILDREN.

By S. J. MELTZER, M.D.,
OF NEW YORK.

In the course of the last fifteen years I have observed a number of cases of lobar pneumonia in children, at the beginning of which earache was the first and predominant symptom. The following two cases occurred a few months ago.

In the last week of December, 1898, the three children of the family of G. became sick with coryza, pain in the throat, moderate hoarseness, barking cough, and a temperature varying between 100° and 101°. These symptoms disappeared after a week's duration. The oldest boy, seven years old, had had twice purulent otitis media and numerous short attacks of earache since his second year, but was free of them for the last two years, since his tonsils and adenoids were removed. The second child, a boy of five years, had never had earache, nor has he adenoids or large tonsils. The third, a baby of twenty months, has since last fall had two attacks of earache with a temperature of 101°, each attack lasting five to six days, and terminating apparently in perfect recovery. In the first attack the pain was confined to the left ear alone; in the second attack both ears were involved, with apparently equal intensity. On January 30th the baby began to scream with pains in the left ear, and the temperature rose at once to 103°. In the course of the day the right ear also became sensitive to touch, while the pains in the left ear appeared to be somewhat lessened. Respirations were only 26 per minute, and there was no cough or any physical sign to suspect the respiratory organs as the seat of the main cause of the fever. On the second day the temperature rose to 104° in the morning and 105° in the afternoon; the respirations gradually increased in number and reached 40 per minute on the fourth day; on the third day the characteristic moaning appeared on the scene, and on the fourth day the posterior surface of the lower right lobe presented all the physical signs of consolidation. The earache diminished from day to day, and disappeared entirely with the onset of the crisis, which took place at the end of the fifth day.

On January 31st, just twenty-four hours after the onset of the pneumonia

in the baby, the oldest boy commenced to complain of a severe pain in the left ear, the same one which was affected in the previous years, had a slight short chill, and the temperature rose to 103°. His hearing was apparently not impaired. About sixteen hours later he began to complain of a pain in the chest, locating it in the axillary line about the fifth intercostal space, and on the following day there were dulness and bronchial breathing over the left lower lobe. Here, too, the pneumonia ran a course of five days, but the earache already disappeared entirely on the third day.

In December, 1884, I was called to see Leonard A., a boy of four years, who had already been sick for three days. It began, I was told, with a sudden onset of high fever and severe pains in the right ear, and the physician in charge diagnosticated it as otitis media. Next day the earache became less pronounced, but the child began to have a pain in the region of the liver, and in addition to that there was some vomiting, which caused my predecessor to change his previous diagnosis to that of gastric fever. When I saw the child the ear was still moderately sensitive, but the rapid respirations suggested the lungs as the seat of the trouble, and the examination revealed, indeed, a well-marked lobar pneumonia located in the lower right lobe. This experience recalled to my mind a case which I had seen in my office a few weeks before. The child had high fever and earache but no other symptoms. I diagnosticated it as otitis media. When, however, it was reported to me that after the child had taken my medicine for two days it became well all at once, I knew that something must have been wrong with my diagnosis. In the light of my new experience I was inclined to believe that it was a case of so-called central pneumonia, and that there might, indeed, be some causal connection between lobar pneumonia and earache. The pneumonia in Leonard A. had a protracted course and terminated in a crisis on the fourteenth day of the disease; the earache, however, had already entirely disappeared on the sixth day. The coincidence of earache and pneumonia must have made a deep impression also upon the mother of this little patient, for a year later she sent for me to see Leonard, who had, as she stated, pneumonia again. And to my query how she had made out her diagnosis, she answered that the boy started, as in the last attack, with high fever and earache. And, indeed, there were severe pains in the same ear as in the last time, and on the third day there was a well-marked pneumonia in the right lower lobe, which terminated this time on the seventh day of the disease.

Since this first observation I have met with a considerable number of similar cases. They all had in common the following points: At the onset of the disease earache was a predominant symptom; this predominance, however, never lasted longer than one day. Either the pain had already disappeared entirely on the second or third day, or it lost its intensity and finally disappeared, either shortly before the crisis set in or with it. In none of the cases did the pain outlast the

disease; in none did the earache terminate in a discharge from the ear. I should already remark here that I never have observed a suppurating otitis during the course of a lobar pneumonia in children. With two exceptions the earache was on the same side with the pneumonia. As far as I could ascertain all the cases of lobar pneumonia with an initial earache occurred in children who had had, at some previous time, an otitis media in the now aching ear. In children in whom the acuteness of hearing could be tested, the hearing seemed to have been unaffected, even during the acme of the pain.

The age of the children upon whom these observations were made varied between eighteen months and eight years. The initial pain seemed to be the more intense the younger the child.

Besides these cases with a pronounced initial pain, I could sometimes establish in cases of pneumonia in infants a greater sensitiveness of the ear of the afflicted side.

The literature contains some startling statements with regard to the frequency of otitis media in young children, which is not yet sufficiently taken into account by the general practitioner. Already, as far back as 1859, Tröltsch[1] reported that in 25 autopsies of babies he found otitis media 15 times. In 1868 Wrede[2] reported from the Foundling Asylum at St. Petersburg that in 80 autopsies there were pathological changes of the ear in 84 per cent., and Kutscharianz[3] soon followed with reports from the Foundling Asylum in Moscow, stating that in 300 autopsies only 70 children showed normal conditions of the ear. For some time these statements were met with the peculiar interpretation that pus and mucus might be normal constituents in the ears of infants. Within the last decade, however, a number of careful observations have been published, which leave no doubt of the pathological character of the alterations in the middle ear. In 20 autopsies on infants, Netter,[4] of Paris, found true pathological changes in the ears of each and every case. Kossel[5] reported from Koch's Institute in Berlin that in 108 autopsies there was in the ears of 85 infants true otitis media containing bacteria, mostly of the same kind which were found in the main disease of which the child died. Rasch[6] reported from the hospital in Copenhagen that out of 61 necropsies otitis media was found in 56 of the children, out of which number 32 had true abscesses in both ears. And quite recently

we read in a communication from Ponfick,[7] the well-known pathologist of Breslau, that in 100 consecutive autopsies of children who died from one or another disease, the ears were normal in only 9 cases; in the remaining 91 a well-marked otitis media of a purulent or mucopurulent character was present.

In the great majority of the cases reported by the different writers the presence of otitis media as a complication of the main disease was not recognized during life, a fact which finds an easy explanation in the following circumstances: In diagnosing otitis media we have to rely upon the presence of an earache, on an otoscopic examination of the drum, and on the appearance of pus in the external meatus. Of the presence of an earache the baby tells us loud enough indeed by its screaming, but we all know that not only the mothers, but also the doctors, mostly attribute such screaming to intestinal colic—until the appearance of pus on the pillow clears up the diagnosis. It was just such an experience in the family of Prof. Ponfick that caused him to examine systematically the ears of dead infants. As to the otoscopic examination of the drum, it is admitted even by the expert otologist that in infants it is a difficult and unsatisfactory task, on account of the narrowness of the canal, the nearly horizontal position of the drum, etc. There remains then only the appearance of pus in the outer ear to rely upon for a sure diagnosis of the existence of an otitis; but here the report tells us an interesting fact. In the 85 cases of Kossel there were only 3 perforations of the drum; of the 56 cases of Rasch there were only 4 perforations; in short, all the reports testify that there is very little tendency in these cases of purulent otitis to perforate the drum—either, as some say, because the pus lacks the corroding quality, or, as others say, because the Eustachian tube is so wide in infants as to offer to the pus an easy outlet into the pharynx.

Recently, however, a few reports were published from pediatric institutions in which the diagnosis was made *intra vitam.* These reports, too, show the great frequency of otitis in children. Hartmann[8], a well-known otologist in Berlin, reports that he had made in Koch's Institute an otoscopic examination of 48 children and recognized otitis media in 38 of them, and in nearly all the cases the diagnosis was verified by the postmortem. He makes the significant statement that in the beginning of the main disease the drum did not

yet show any pathological changes. A similar report is made by Goeppert[9] from Heubner's clinic. From 73 children who were examined otoscopically in 59 the drums have shown the pathological changes of otitis. All of them came to autopsies, which, with a few exceptions, confirmed the diagnosis of otitis.

All these reports have in common that they came from such institutions where the little inmates are mostly very poorly nourished, atrophic creatures who invariably end their career on the postmortem table. There is, however, one report of a series of observations which were made on a better class of children. This report has the advantage and disadvantage that no postmortem verified the diagnoses, which were made on the strength of otoscopical examinations. The report is made by Teichmann,[10] from Neumann's Ambulatorium for Diseases of the Air-passages in Berlin. In just one-half of the 268 children who suffered from various diseases of the air-passages, the main diseases became earlier or later complicated by otitis media.

An examination of the above-quoted reports with regard to the relation of pneumonia to otitis shows that in the cases of Wreden and of Kossel otitis was mostly complicated with broncho-pneumonia; in the 20 cases of Netter 14 had catarrhal pneumonia. We read in the report of Rasch that in 43 cases of broncho-pneumonia 42 were complicated with otitis media; of 36 cases of otitis reported by Hartmann 24 suffered from catarrhal pneumonia; of 11 cases of pneumonia in Ponfick's autopsies 10 had purulent otitis in both ears; and of 73 cases of pneumonia observed by Teichmann 34 had otitis. Thus we see that otitis media is a very frequent complication of catarrhal pneumonia in children. But how about lobar pneumonia? Except Ponfick and Teichmann, all the writers expressly speak of broncho-pneumonia, and no mention is made of lobar pneumonia. Ponfick and Teichmann speak of pneumonia without specification. Ponfick, however, speaks of his cases of pneumonia as having been of a lobular and confluating character, and apparently means also broncho-pneumonia. In Teichmann's report alone we find no hint as to the nature of the pneumonia which he had under his observation, and we probably do not err in assuming that his 73 pneumonias include also cases of lobar pneumonia. We have, however, no means of establishing whether there was any lobar pneumonia among the cases which were complicated with otitis media.

In the literature on lobar pneumonia in children which I had a chance to examine I found no mention of otitis media as a complication of this disease. Should lobar pneumonia be exempt from this complication? I have already mentioned above that in all the cases of lobar pneumonia in children which came under my observation I never have seen a discharge from the ear setting in during the course of the disease. This alone, however, cannot be taken as a sure proof that a purulent otitis does not exist at the same time, since we know from the above cited reports that the purulent otitis in children has very little tendency to perforate the drum, and this is especially the case, at least as Rasch claims, in those cases of otitis which are caused by the pneumococcus. I have, however, made two observations which seem to show that there is indeed a certain antagonism, in children at least, between lobar pneumonia and purulent otitis.

Adeline L., aged two years, had, after recovering from laryngeal croup, an attack of otitis media which terminated within two days in a purulent discharge from the ear. The discharge continued to be profuse for five weeks, when the child was suddenly seized with a chill and a rise of temperature to 104°. On the very same day the discharge stopped entirely. On the second day physical signs of lobar pneumonia appeared. The disease lasted twelve days, and during this period there was no sign of a discharge; but one day after the defervescence took place the purulent discharge reappeared again.

The second case was that of a boy of five years who had a "running" ear of long standing. When, one day, there was a sudden rise of fever with a simultaneous disappearance of the discharge and the appearance of a pain in the same ear, I was at first inclined to believe that the fever was due to the retention of pus within the ear. But the appearance of the signs of consolidation in the entire left lung cleared up the diagnosis. The earache disappeared on the third day. The pneumonia lasted nine days, and a discharge did not reappear until four days after the crisis.*

These two cases remind one of the observations of Bogdan[11] and of Hymanson,[12] who reported cases of gonorrhœa, the discharge of which disappeared with the onset of a lobar pneumonia and reappeared again during convalescence.

This disappearance of a purulent discharge during an attack of pneumonia is apparently not an accidental occurrence, and might

* The following case occurred recently in the practice of Dr. Victor Meltzer: Emma R., two years old, had double purulent otitis for about two months When, at the beginning of May, she developed lobar pneumonia, the discharge stopped in both ears and did not return until three days after the crisis.

perhaps be explained by the appearance of hyperleucocytosis in the disease of pneumonia; the secreting mucous membranes are hereby cut short of their supply of leucocytes.

The usual disappearance or diminution of purulent bronchial discharge with the onset of a lobar pneumonia is possibly another instance of the antipurulent, drying effect of the lobar pneumonia, and might also be explained by the greater demand of the body upon the limited supply of the leucocytes. We may quote here the statement of Bernabei,[13] that the presence of an abscess in one part of the body presents to a degree an obstacle to the formation of another abscess in another distant part of the body.*

What, then, does the earache mean which I have often observed to appear at the onset of a lobar pneumonia in children? At the time when I had first made my observations, in 1884, a period in which the bacteriology of pneumonia as well as of otitis media was yet unknown, I was inclined to consider these earaches as instances of so-called sympathetic pains. When a stimulus is applied to one spot and a sensation or a pain is hereby felt also in another spot of the body, this sensation or pain is usually termed sympathetic. It is also termed irradiation. The peripheral impulse, after reaching the nerve-cell which is connected by sensory nerves with the first spot, spreads, irradiates from here to a neighboring nerve-cell, and causes there a sensation which is believed to come from the second peripheral spot connected with this second nerve-cell. The irradiation of a toothache to the adjacent normal teeth is an instance of an irradiating or sympathetic pain. This sympathy might even occur between a tooth of the upper jaw and one of the lower jaw, which means that an irradiation is taking place between the nerve-cells belonging to two different branches of the trigeminal nerve. Looking at the bright sun produces a tickling sensation within the nose, and might even cause sneezing, which is another instance of sympathetic sensation irradiating from cell to cell within the nucleus of the trigeminal nerve. Another instance of sympathetic sensation, and one which interests us here, is the known fact that in many individuals stimulation of the external meatus of the ear causes a tickling sensation within the larynx which may even bring out a cough. This means that the stimulus which is

* See also Alfred Stengel (Therapeutic Gazette, February 15, 1898), who reports the favorable effect of an artificial abscess upon pneumonia with delayed resolution.

carried along the auricular branch of the vagus causes in the corresponding nerve-cell a sensation which irradiates to the nerve-cells of the laryngeal superior, another branch of the vagus. As for the initial earache in pneumonia, we might simply turn around the last instance: The stimulus which is caused by the inflammation of the lung is carried along the pulmonary branches of the vagus to the corresponding nerve-cell, causing there a sensation. This is transmitted by irradiation to the nerve-cells belonging to the auricular branch which provides the ear-drum with sensory nerves, thus causing there a sensation of pain which appears to the patient to be in the ear.

However, after a few years of experience, a certain objection to this explanation of the initial earache appeared to grow out of the fact that it nearly always occurred in such ears as had already been at some time or another the seat of an inflammation, a fact which would suggest that the present pain had something to do with the previous inflammation of the ear. On the other hand, the discovery of the pneumococcus as the originator of lobar pneumonia and the statements of Zaufal,[14] Netter,[15] and others that the pneumococcus is also frequently the cause of otitis media, and the further statement by Netter that the pneumococcus is often a common inhabitant of mouth, nose, and throat of healthy children, have suggested the possibility that accidentally the pneumococcus might enter simultaneously the lungs as well as the middle ear, causing a simultaneous inflammation in both places, which would thus satisfactorily explain the appearance of an earache just at the onset of a pneumonia. The fact that the earaches never resulted in a serious otitis with a perforation of the drum, need not speak against this assumption, as it could be explained by the suggestion made above, that the lobar pneumonia with its hyperleucocytosis acts as a derivative upon the inflamed tympanum. This interpretation would reduce the initial earache in lobar pneumonia to a mere accidental coincidence. However, while it must be admitted that such coincidences are indeed liable to occur, the interpretation of all these cases of an initial earache in pneumonia would be open to the criticism: Why should the accident of an infection of the tympanum be confined exclusively to the onset of the pneumonia and never occur after, and rarely a few days before, the onset? Furthermore, cases like the following seem to speak positively against the theory of an accidental coincidence.

Nettie H., aged twenty-six months, had at the middle of November, 1892, as the mother stated, a common cold, which got better within a week. On December 2d I was called to see her on account of an earache which she had since the day before. The right ear, which I found covered with a flaxseed poultice, was moderately sensitive, but the mother assured me that it was much worse on the previous day, and that in her opinion the relief came from the poultice, which used to relieve the same child in previous attacks of earache. The temperature, however, was 105° F. and the respirations 40 per minute. I pronounced the disease as pneumonia, and on the fourth day there were all the physical signs of a consolidation in the right lower lobe. The earache subsided on the fifth day, and the pneumonia terminated in a crisis on the seventh day. For two days the child felt quite comfortable. On the tenth day of the disease it had again a severe earache, and again on the right side, and the temperature rose at once to 103° F., and already, on the second day, there was a marked consolidation of the right upper lobe. This time pneumonia and earache disappeared simultaneously on the fifth day.

Surely, it would be going too far to maintain that the earache at the onset of the second attack in this case of migrating pneumonia was due to a second accidental simultaneous invasion of pneumococci in the middle ear. I shall confess that my own belief in the existence of a causal connection between earache and pneumonia goes so far as to risk a diagnosis of pneumonia already on the first day, when, outside of the high fever and frequent breathing, there is nothing else but a severe earache, and so far I was never yet put in a position to retract such a diagnosis.

My present attempt to offer a more satisfactory interpretation of the phenomenon of an initial earache in lobar pneumonia will be based upon a certain form of summation of stimuli, which to my knowledge has never yet been brought forward, and which I will have to discuss here first. If two weak stimuli are applied to the same spot of any part of the body, one after the other within a short interval, they are capable of producing an appreciable effect on the central organ, though each stimulus separately may be too weak to do it; the weak impulses of the two subminimum stimuli are added together within the central organ to the sum-total of an effective stimulus. That is the usual meaning of summation. A summation, however, can take place also when the two stimuli have been applied to two different places of the body, either simultaneously or one after the other. Exner,[16] who has pointed out this form of summation, terms it "Bahnung," which means preparing the way, and exemplifies it by the statement that

when one subminimum stimulus is applied to one leg while the other subminimum electrical stimulus is applied to the cortex, the result is a reflex contraction of the leg which could not have been effected by each stimulus alone. The same summation takes place, of course, also, when each stimulus alone is strong enough to be effective; the summation consists, then, in the greater degree of the effect.

I wish now to point out a form of summation of stimuli which has, as far as I know, not yet been dealt with. It is the summation of an abrupt and a continuous stimulus. We know that a stimulus must have a certain abrupt increase in intensity to be effective. If heat or pressure, applied to some part of the body for the purpose of producing a stimulus, would increase very slowly, they would neither produce a sensation nor a reflex contraction. The same is the case with an originally effective stimulus if it continues for some time with unchanged intensity, only the abrupt onset of the stimulus is effective, not its unchanged continuation. The impulses generated by such continuous stimuli are nevertheless not lost to the central organ, and by the addition of an abrupt but subminimum stimulus these impulses can be made to be very effective. I shall take my instances from pathology. Hyperæsthesia means such a summation. The continuous stimulation of a certain spot in the body by an acute or chronic inflammation may not produce a special sensation; a slight touch, however, will cause quite a strong sensation; the touch of the head of a pin is felt in such a hyperæsthetic area like the prick with the point. It means that the impulses generated by the subminimum continuous stimuli are added within the central organ to the new abrupt stimulus. This instance presents a summation of stimuli coming from one and the same spot. However, as it is the case in the summation between abrupt stimuli, a summation between the continuous and the abrupt stimuli takes place also when both stimuli are coming from different localities. The meeting of the impulses of these stimuli within the central organ might take place either by special intracentral paths or by the general way of irradiation as described above.

The following instance will illustrate these conditions: I am subject to alveolitis in all of my incisors, and at all times they are in a state of hyperæsthesia. Now, when I use a spray of a concentrated solution, say of antipyrin, in my right nose, I experience a pain in the right incisor which is even stronger than the pain in the nose itself.

The pain in the incisors is due to the summation of the continuous stimuli from the chronic alveolitis with the abrupt stimulus applied to the nose, the impulses of which, after travelling along the nasal nerve branches and reaching their nerve-cells, irradiate to the cells connected with the dental nerves. If the solution is less concentrated it may happen that the incisors are the only place where a pain is distinctly felt. The pain may irradiate even to the other incisors, and if a more or less acute alveolitis is present in the lower left incisors it might happen that it is there where the pain is mostly pronounced after spraying the right nose. In this case the irradiation not only spreads from the second to the third branch of the trigeminus, but it even traverses the middle line in order to form a union with the impulses of the continuous stimulation coming from the inflamed area of the left side. I have often seen a moderate coryza causing considerable pain in the lower teeth when they are the seat of some chronic process. The stimulating effect of the coryza alone was too weak to cause a sensation of pain in the nerve-cells belonging to the nasal nerves, but it aided the continuous stimuli from the irritated lower teeth to be felt as a distinct pain.

Without entering here into a further discussion of the extensive applicability of our new point, we shall see now how the initial earache in lobar pneumonia can be explained by the summation of the abrupt and the continuous stimuli. We have seen above that the initial earache occurred in such ears as at some previous time were the seat of an acute otitis media. We know that the drum is almost always involved in acute otitis. We may further presume that after the subsidence of an acute attack, at least in many cases, a chronic otitis and myringitis may persist for some time without showing a distinct pain or a discharge, which persistence explains the readiness of such ears to respond with an acute otitis to the slightest provocation. If now, in individuals afflicted with such a chronic myringitis an acute inflammation of the lungs sets in, this inflammation stimulates the pulmonary branches of the vagus and sends up impulses to the cells of these nerves from where impulses irradiate to the nerve-cells of the auricular branch of the vagus. Here they find the continuous impulses from the chronic myringitis with which they form a summation, with the result that the new pain is experienced in the ear. It is exactly similar to the pains in chronically afflicted teeth at the onset

of coryza. As long as the inflammation of the lungs increases in intensity and involves new areas the sympathetic pain is kept up by the new abrupt impulses which are constantly sent up along the pulmonary nerves. When the inflammation assumes a stationary character the abrupt stimuli cease, and with them disappears the sympathetic earache. The inflammation sometimes also causes pain in the lungs themselves; but it seems that this occurs only when the inflammation reaches the pleural surface; the parenchymatous tissue of the lungs does not seem to be very sensitive to pain, which is in conformity with the behavior of other viscera—the abdominal, for instance.

My paper brings out the following points:

Otitis media is an extremely frequent disease in children, especially in poorly nourished ones.

Broncho-pneumonia is very frequently complicated with otitis media.

In lobar pneumonia of children purulent otitis media is at least very rare, possibly because the pneumonia by its hyperleucocytosis acts as a derivative upon the otitis.

Many cases of lobar pneumonia commence with an earache, which disappears gradually.

The hypothesis is offered that possibly this is only a sympathetic pain of a chronically inflamed drum.

In offering this hypothesis the idea is introduced of a summation within the central organ between the effects of an abrupt and of a continuous stimulus, a conception which might prove to be fruitful in pathology where all the chronic and many acute inflammations are the seat of such continuous nerve stimulations.

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DISCUSSION.

DR. JACOBI: So far as I understood it, the doctor had no symptom of otitis media except that of pain. He explicitly stated that there was no perforation of the drum membrane, no pus in the ear, and, of course, no pus was observed in the throat. I would suggest that the presence of otitis media in those cases in which no pus is seen can hardly be proved. What can be proved is only the pain, high temperature, and succeeding pneumonia. The doctor has not told us, at least, I did not hear it, about the condition of the throat. If I were permitted to throw out a suspicion as to the nature of the pain, I might suggest that the earache was simply one of the symptoms of an angina. That is merely a suggestion, and may be all wrong, but as long as we cannot prove the existence of the otitis some of the cases may be explained in that way.

DR. KINNICUTT: I think this is a most interesting communication; but as the paper was read it occurred to me that the great frequency of otitis media observed in children dying from all causes rather militated against the idea of a connection between otitis media and lobar pneumonia.

DR. JACOBI: May I add a word in connection with the remark just made? It is this: the question whether at autopsy an abnormal or apparently abnormal condition of the middle ear in small children is normal or pathological does not appear to be altogether settled; at all events, the presence of bacteria in the middle ear should not be claimed as proof that there is an infection due to them. We do not diagnosticate diphtheria every time we find diphtheria bacilli in the throat, or tuberculosis of the nose or throat simply upon the finding of tubercle bacilli. A great deal more is required, and the presence of bacteria in the very accessible middle ears of infants does not prove that they constitute a part of a morbid process. The fact that there is a great deal of mucus or muco-pus in the middle ear does not prove altogether that there is an otitis, just as we do not make a diagnosis of rhinitis upon the finding of mucus or muco-pus in the nasal cavities. While I am not prepared to say that those who consider the presence of muco-pus as absolutely normal are correct, neither do I think those who consider it necessarily part of a morbid process are absolutely correct. It has occurred to me that what in the adult appears to be the result of inflammatory processes need not be so in children, because the middle ears of the latter are so very accessible to injury from outside and to infection from the pharynx.

DR. ROTCH: It is very important to recognize the great frequency of affections of the middle ear in young infants, for it is often found that there is some affection of the ear, usually purulent otitis, in connection with many diseases. I have found it necessary in the last few years to have a routine

examination of the ears made at least once a week at the Infants' Hospital, because the infants may be losing in weight from the drain made upon them by an otitis media, without any symptoms that would call attention to it. Many of these young infants have no pain whatever. It is a very easy matter in most institutions to have such routine examinations made by competent men.

DR. MELTZER: I shall first answer Dr. Kinnicutt's question. I think I have stated my reasons for assuming that otitis media does not occur in lobar pneumonia of children. All the reports which speak of otitis as a complication of pneumonia mention expressly broncho-pneumonia, and I did not find a single case of otitis mentioned in connection with lobar pneumonia. I have looked for it for many years in a large number of cases of lobar pneumonia, but have never yet observed a case of purulent otitis complicating this disease.

In regard to Dr. Jacobi's remark as to the frequency of otitis media in infants, that perhaps the products which were found in the ears of the dead infants were not due to some inflammation, but are normal constituents of the infant ear, I will admit that in previous years this position was held, indeed, by many well-known writers. Within the last ten years, however, very careful studies have been made of the subject by pathologists competent of distinguishing between the normal and pathological conditions, and it has been established that the changes in question present a real otitis. Furthermore, when the main disease of which the child died had a characteristic micro-organism as its cause, this same organism was found in the pus of the otitis; the pyocyaneus which produced an enteritis in one case was present also in the pus of the otitis, and I think it is considered now an established fact that the otitis found to be so frequent in children is a real otitis media and not a natural condition.

REPORT OF FIVE CASES OF ENDOCARDITIS OCCURRING IN THE COURSE OF TONSILLITIS.

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ONE of the most interesting questions in medicine at the present time is the etiology of acute articular rheumatism. Each year there is a steadily growing assurance that it should be classed among the acute infections; and, while it cannot be said that as yet the causative agent has been found, our knowledge is in reality more definite in regard to this disease than it is in respect to scarlatina and many of the other well-recognized infections. It is as a slight contribution to our knowledge of what might be called collateral evidence of the infectious nature of acute articular rheumatism that the present report is made. The subject of the pathogenesis of acute articular rheumatism, and its allies among the "rheumatic group," was at first thought of by me as the text of a paper before the Association; but a discussion of the subject, as a whole, would have far exceeded the proper limits of such a paper, and I decided to simply make the subjoined report, reserving for another occasion the account of examples of other associations of this interesting "rheumatic group of diseases."

In offering this report, I must express my regret that in none of my cases was a bacteriological examination made to determine the causative agent of the angina.

CASE I.—L. S., white, aged four years, had been under my care during 1893 for one or two slight acute and transient ailments. He had been several times thoroughly examined on these occasions without the discovery of any abnormality except the signs of his various slight illnesses. On Christmas day I was sent for to see him because of anorexia and fever that had come on acutely on the morning of that day. I saw him in the afternoon, and found that he had an axillary temperature of 102.6°, and that the right tonsil

was slightly inflamed and that there was an enlarged lymph-node at the angle of the right jaw. On the next day I noticed that there was slight "cardiac excitement," although the temperature had fallen to 99.2° and the throat looked much better. On December 27th I made the note that he had had a bad night. His temperature was, when I saw him, 101.2°, the pulse 108. The gland at the right angle of the jaw was rather larger, although the tonsil looked perfectly well. At the apex there was a whirring systolic murmur of short duration. Under the right clavicle there was a loud, whirring systolic murmur almost continuous, and sounding almost precisely like the venous hum of anæmia. The same hum was heard close to the sternum on the left side just below the clavicle. At the same time auscultation of the neck showed the presence of a loud, roaring continuous murmur over the enlarged gland. That night he suddenly awoke, complaining of pain in the region of the heart. When I saw him on the afternoon of the 28th his general expression was better, his temperature a degree lower, his pulse 110. His apex-beat was found to have travelled to the left and to be 4 cm. to the left of the left nipple line, while the right border of cardiac dulness was at the left sternal border. At the apex the harsh systolic murmur was still present and well transmitted for a short distance to the left The same humming murmurs were present at other situations as on the previous day.

From this date the course was one of steady improvement. The temperature fell to normal by January 1st, and the general condition rapidly improved. With the subsidence of fever the humming murmurs below the clavicles and over the glandular swelling disappeared. The pulse continued to be irregular in force and rhythm and the heart readily excited, so that confinement to bed was continued for two weeks after the temperature fell to normal and until the heart's action ceased to be affected by change of posture. The apex beat gradually but steadily returned to the normal position. The rough murmur persisted at the apex, and was heard to the left. This cardiac condition remained until he passed from under my immediate observation on going to the seashore.

I again examined him in December, 1894, because of the persistence of the glandular swelling and of an attack of acute bronchitis. Examination of the heart then, one year after his illness, showed the presence of a blowing systolic murmur at the apex, well transmitted to the left anterior axillary line, of accentuation of the second pulmonary sound, and the right border of cardiac dulness at the right edge of the sternum, the apex-beat being in the normal position.

The presence of such an apical murmur as that described would, of course, not prove the presence of endocarditis any more than would the presence of the venous murmur beneath the clavicles prove organic lesion, as these latter are of great frequency as transient phenomena in many acute illnesses of childhood, and are of little significance. The persistence of the apical murmur, its transmission to the left, the

accentuation of the pulmonary second sound, and the extension of cardiac dulness to the right one year after subsidence of the acute process, show that organic change was present at the mitral area, probably a mitral valvulitis.

CASE II.—D. W., white, aged fourteen years, school-girl, had been several times under my care for slight ailments over a course of four or five years, and had never presented signs or symptoms of cardiac lesion. In 1894 she had a mild attack of angina with catarrhal inflammation of the pharynx. For several days thereafter the heart's action was quite irregular, but finally became steady. During and after this attack the heart-sounds were entirely free from murmur or other evidence of organic change. On October 11, 1895, I was asked to see her because of pain on swallowing, noted that morning. The apparent cause was chilling from sleeping under too few coverings. There had been no rigor and no sensation of fever. All of the structures of the throat were found to be intensely red and dry. The pulse was 108, the temperature 100°. On auscultation of the chest there was found "over the body of the heart a somewhat musical systolic murmur with a rather 'whipping' character." Under treatment the angina promptly disappeared, but the murmur continued, and my notes describe its characters and localization as follows:

On October 12th it was still heard over the heart, and had a "swishing" character. On the 14th there was at the apex a loud, clear-cut systolic, rather blowing murmur, well transmitted to the left axillary region. On the 21st the murmur was still very loud and clearly transmitted to the left posterior axillary line. On November 7th palpitation and breathlessness were marked on making a slight but unusual exertion.

On November 9th the murmur was well heard at the lower angle of the left scapula. On November 29th the murmur is described in my notes as very loud, whirring in character, and well-heard, not only in the left axillary region, but also at the scapular angle. Shortness of breath was present on going up stairs, but not at other times. The latter symptom soon subsided, but the systolic apical murmur, with accentuated second pulmonary sound and slight extension of cardiac dulness to the right, are still present after the lapse of four years. Compensation is apparently perfect.

Whether, in this case, the attack of angina in 1894, a year before the appearance of physical signs of organic change, had been accompanied by slight cardiac damage cannot be determined. Possibly the peculiar and marked cardiac irregularity, noted then for the first time, may be an indication of some injury sustained at that time, to which fresh additions were made as a result of the second attack of sore-throat.

CASE III.—Eugene A., white, aged six years, had been feeling badly for a week, with sore throat and fever for four days before I was asked to see him, on October 18, 1894. I had never examined him before, and consequently do not know certainly of his previous condition. He had never been ill, and had had no cardiac symptoms. I found that he had a temperature of 101.2°, greatly enlarged and acutely inflamed tonsils, especially that on the left side, quite profuse sweating, but no swelling, pain, or tenderness of the joints. On examining the chest there was found the following condition: The apex-beat was in the normal position. Distinct pulsation could be seen and felt over the whole præcordial region. Cardiac dulness began at the third rib in the left parasternal line and at the mid-sternum at the level of the fourth interspace. No thrill could be felt. In the whole region of the apex-beat there was a harsh, rasping, systolic murmur transmitted best toward the left, but heard with diminishing intensity as far to the right as the root of the xyphoid. The throat rapidly improved and the general symptom steadily subsided, but the heart condition remained the same. On October 24th, about a week after my first visit, I made the note that the apical systolic murmur persisted, but that within forty-eight hours there had developed between this and the preceding visit a harsh, low-pitched systolic murmur heard best at the aortic area and transmitted into the carotids, and also a distinct to-and-fro friction sound, which was best heard just within the apex. After a few days the friction sound and the systolic aortic murmur disappeared, and there developed a presystolic murmur at the apex. The double murmur at the apex continued long after all other signs of illness had disappeared. I again examined him at the end of a month, and made the note that the apex-beat was at the junction of the fifth interspace and the left mid-clavicular line, that the cardiac dulness began at the upper border of the third rib in the left parasternal line and at the right border of the sternum, and that there was a crisp presystolic and blowing systolic murmur at the apex, with accentuation of the pulmonary second sound.

Occasional subsequent examinations during the next year showed persistence of these signs. While the condition of the heart before this illness is not certainly known, he had never shown any symptoms of cardiac trouble, and had had no previous rheumatism, scarlatina, or other of the diseases likely to produce endocarditis. The progressive addition of signs of recent endopericarditis tends to strengthen the probability that the whole process was of recent origin, and was an immediate result of the throat trouble.

CASE IV.—Andrew S., white, aged thirty-two years, was admitted to the Philadelphia Hospital, under Dr. Musser's care, on December 11, 1894, and through the latter's kindness was frequently examined by me. He had never had rheumatism, and had at no time suffered from cardiac symptoms. A

week before his admission he began to have malaise, loss of appetite, and headache. Five days before admission he had a slight chill, soon followed by pain and difficulty in swallowing. He had no articular pains. On examination the mucous membrane of the fauces and pharynx was found to be swollen and reddened, and the submaxillary lymph-nodes were plainly enlarged. The apex-beat was in the fifth interspace, a half-inch to the inner side of the left vertical nipple line. The area of cardiac dulness was normal. No thrill was present. At the apex there was a low-pitched, rumbling, plainly presystolic murmur, followed immediately by a low-pitched systolic murmur well transmitted to the axillary region. In addition to these murmurs there was a high-pitched musical sound, occurring during the latter part of the systolic murmur, heard best just to the right of the apex, and not transmitted. The latter murmur was transient, but was heard at odd times on several occasions. Four days after admission, after the throat condition had greatly improved, there appeared quite severe pain in the right arm on motion, with tenderness over the nerve trunks. On this day the notes state that the three abnormal sounds in the region of the apex were well heard, although on the day before the musical sound late systolic murmur could not be detected. While the presystolic and systolic murmurs persisted until his discharge, on January 18th, the musical note was still as inconstant as before.

I saw this patient again in the latter part of July, 1896, a year and a half after his first coming under observation. He was then in Dr. Lewis's ward at the Pennsylvania Hospital, to which institution he had been admitted for malaria. Examination then showed that the apex-beat was diffuse, but with its greatest impulse in the fifth interspace 10 cm. from the mid-line. There was a faint suspicion of a presystolic thrill at the apex. The cardiac dulness began at the lower border of the third rib in the left parasternal line, and a trifle to the right of the right sternal border at the level of the fourth interspace. There were present a presystolic and a systolic murmur, the latter being well transmitted into the axilla, and heard at the left scapular angle. On a second examination, after a few days' rest in bed, the presystolic murmur could not be heard on one occasion.

While incapable of positive proof, the heart in this case was presumably healthy before his tonsillitis, and the latter either originated or aggravated an endocarditis.

Case V.—In November, 1895, I was asked to see E. R., white, aged five years, whose regular medical attendant was out of town. I found that he had been well all summer, but that a few days before I was called he had suffered from a slight sore-throat, of which there was a small epidemic through the household. My services were asked because of the appearance of a glandular swelling on the left side of the neck that had been first noticed on the evening before. On examination I found an enlarged and tender

lymph-node below and behind the left ear. There was no visible trouble in the throat, ear, or scalp. On listening to the chest I found a short, musical, systolic murmur, with its point of greatest intensity at the apex, and well transmitted to the left anterior axillary line. There was no change in the area of cardiac dulness. I saw him once or twice within the next few days, but upon the return of his regular medical attendant, transferred him to his care. The exact subsequent heart condition I do not know, but I heard from his mother that during the succeeding winter his physician had given such directions regarding exertion as pointed directly to the persistence of signs or symptoms of an impaired heart.

While I had never listened to this child's heart before the occasion of this visit, I could obtain by close questioning no history of past illness likely to cause, or of preceding symptoms pointing toward, any cardiac trouble.

The first question that arises in regard to these cases is the value of the evidence of the existence of endocarditis. I have gone a little at length into the subsequent history of some of them in order to show that the physical signs were persistent, and that subsequent changes in the cardiac outlines and other signs were precisely those that would convince us of the presence of mitral valvulitis as a result of a frank attack of acute articular rheumatism had that been the acute illness from which the condition dated.

In all these cases careful inquiry into the past history failed to reveal any articular pains, and careful examination showed no present signs of joint trouble. They were manifestly, therefore, not to be classed as cases of acute articular rheumatism, with slight joint manifestations. I feel satisfied as to the immediate dependence of the changes in the heart upon the angina. In most of the cases I had found the heart normal before the illness; in the others the evidence would point toward at least marked increase, if not origination, of endocardial change by the tonsillitis or pharyngitis. In other cases I have strongly suspected the tonsillar origin of endocarditis; but, as the connection could not be proven, I have not added them to this report.

If it is granted, as I think it must be, that these are truly cases of endocarditis, their exact position becomes a matter of some interest. It might be said that the tonsillitis and the endocarditis were simply "rheumatic," and that the cases were examples of larval, latent, or abarticular rheumatism. Such an explanation is by no means

satisfactory. In the individual cases there was no preceding history of any of the ordinary rheumatic manifestations, and in the subsequent history of those that I have been able to follow up there have been at no time any evidences of the presence of other members of the "rheumatic group."

I believe these cases to have been plain cases of acute tonsillitis and pharyngitis, having no connection with rheumatism, and that the endocarditis arose as a direct consequence either of infection of the endocardium by micro-organisms, which gained entrance by way of the tonsils, or of structural change in the mitral leaflets, brought about by coagulation necrosis or other result of the chemico-vital action of toxins produced by micro-organisms present in the throat and absorbed from the inflamed tissues. In support of the former theory of their causation, I would here refer only to the fatal case reported by Charrin in *La Semaine Médicale* for 1897, p. 105, where, in an autopsy upon a fatal case of tonsillitis, the staphylococcus aureus was found both in the tonsil and in the vegetations upon the valves of the pulmonary artery. The only connection that I can see between these cases and rheumatism is in the fact that the tonsillitis and pharyngitis in any of them *might* have been followed by arthritis.

Tonsillitis as a cause of endocarditis is but rarely mentioned in text-books and monographs upon medicine or diagnosis. In looking over most of the standard works of reference and text-books that would mould the thought of student or practitioner, I find that most of them speak of tonsillitis as one of the rheumatic series, and note the possible association of any two of the series apart from any articular manifestations. To my mind this view is not satisfactory, and is based upon the theoretical assumption of a specific poison of rheumatism which can attack various tissues. It would seem far more rational to look upon tonsillitis as an infection (which it undoubtedly is), and to view the endocarditis or the arthritis alone or in combination as the direct and immediate result of the entrance of micro-organisms through, or absorption of toxins from, the tonsil or pharynx.

The occurrence of endocarditis as a direct complication or result of tonsillitis is, however, noted by a few writers without the "rheumatic" explanation. Osler, in his *Practice of Medicine* (pp. 452, 699), mentions the association. Dupré (in the *Traité des Mal. de*

l'Enfance, vol. xi. p. 399) speaks of the cases mentioned by Fränkel, Fürbringer, and Sallard.

In Loomis and Thompson's *System of Practical Medicine* mention is briefly made as to this association by R. C. Cabot in his article upon acute follicular tonsillitis, and by A. L. Loomis in the section upon endocarditis.

A. Ruault, in the *Traité de Médecine of Charcot, Bouchard, and Brissaud* (T. iii. p. 63), in discussing acute non-specific angina, mentions Fränkel and Fürbringer's cases of ulcerative endocarditis, but says nothing further.

Whittaker, in vol. iv. of the *Twentieth Century Practice of Medicine*, p. 156, says: "The tendency of modern belief is to regard the throat as the avenue of entrance for the micro organisms of rheumatism, and endocarditis has been reported in the course of both simple and epidemic tonsillitis (quinsy)," and on page 147 says also: "The fact that endocarditis may precede the rheumatism, and that either affection may exist independently of the other, has developed the belief that neither one of these affections causes the other, but that both are effects of a common cause." Pott (*Fortschritte der Medecin*, vol. xiii. Nos. 22 and 23), in speaking of the etiology of heart disease in early childhood, speaks of the occurrence of endocardial and pericardial inflammation after an acute fever with angina, but without fixed articular pain. He, however, apparently looks upon these as "larval forms" of rheumatism, as do so many other writers, and an enumeration of them would be useless waste of space.

Haig-Brown (*Lancet*, October 2, 1886, p. 635, and *Medical News*, January 8, 1887, p. 44) found conclusive evidence of endocarditis—*i. e.*, persistence of signs of organic valvular disease—in 8 out of 345 cases of tonsillitis, while in 3 of the 345 cases pericarditis developed.

Boucsein (*American Journal of the Medical Sciences*, October, 1889) reports two cases of tonsillitis with the development of an apical systolic murmur during the course. Whether these murmurs denoted the existence of endocarditis may possibly be doubtful, as both murmurs disappeared—one in two weeks and the other in four weeks—although the tonsillitis in each case ceased within a few days. He mentions another case with mitral insufficiency, without history of any previous illness save tonsillitis. Of course, direct proof of the dependence of the lesion upon the tonsillitis is in this case insufficient.

In an article upon the bacteriology of angina in the *Annales Suisses des Sciences médicales* for 1895 (abstracted in the *Rev. mens. des mal de l'Enfance* for August, 1896, p. 398), Max Stoss mentions two cases of angina accompanied by endocarditis, the causative agent of the former being in one case the streptococcus pyogenes alone; in the other that organism associated with the micrococcus conglomeratus.

Charrin's case (already referred to) was one of tonsillitis followed by broncho-pneumonia and death. At autopsy the liver was fatty, the spleen soft, the right lung the seat of broncho-pneumonic patches, and there were exuberant vegetations on the pulmonary valves. The staphylococcus aureus was found on the tonsils, in the broncho-pneumonic patches, and in the vegetations on the pulmonary leaflets. Here the most probable sequence was tonsillitis, infection of the pulmonary valve leaflets, broncho pneumonia (?).

Recently Benda (*Riforma medica*, December 13, 1898; abstract in the *New York Medical Journal*, April 1, 1899, p. 460) has reported two cases of ulcerative endocarditis, in one of which the port of entry for the infecting agent was the tonsil.

In a letter to the *Lancet* of January 22, 1881 (p. 154), William Stewart refers to the pyæmic nature of rheumatism, and says that the poison arising from diseases of the throat may miss the joints and expend itself upon other fibrous tissues, and mentions among others the endocardium and pericardium. Apparently, therefore, he can be said to attribute to tonsillitis an etiological relation to endocarditis and to rheumatism as separate complications—the view that I have been endeavoring to support.

An interesting discussion upon tonsillitis, its varieties and relations to rheumatism, was held at the meeting of the Section of Laryngology at the annual meeting of the British Medical Association (*British Medical Journal*, September 14, 1889). At this meeting Haig-Brown spoke of the fact that endocarditis occurs sometimes in the course of tonsillitis, and stated that Dr. Osler had written to him that he had seen two cases of tonsillitis, each complicated by endocarditis, and narrating a third case in some detail. With Haig-Brown's view, possibly since that time modified, that tonsillitis is a general disease, having its chief seat of manifestation in the throat, "as in scarlatina," it is difficult to coincide, as it is more reasonable to suppose that the throat is in many diseases inflamed, because its tissues are the first in-

volved by the infective agents entering the body by way of their surfaces. Archibald E. Garrod, in the same discussion, made a remark that was one of my strongest incentives to the reporting of these cases. I extract the remark in question: "It is sometimes stated that endocarditis may be developed in such cases (sore-throat with articular pains), and even in those who suffer from sore-throat, but have no articular pains. If this can be established a powerful additional argument in favor of the rheumatic origin of the articular pains will be forthcoming. At present, however, the evidence upon this point is still not convincing." Dr. Garrod says, among his conclusions, that when sore-throat is the leading feature of a rheumatic attack there is comparatively little tendency to affection of the endocardium or pericardium. This remark might well hold good if we look upon cases of tonsillitis as the result of a general disease and not as an evidence of the way by which the infecting agent gains access to the body.

R. Hingston Fox at the same meeting said: "With regard to heart-lesions, it is common, even in simple tonsillitis, to find some signs of heart disturbance." He then recounts certain signs which to the doubter would not definitely prove the presence of endocarditis.

DeHaviland Hall, in discussing the subject, mentioned a case of tonsillitis with pericardial friction and an apical murmur.

E Roos (*Berlin. klin. Wochenschr.*, June 18, 1894), in a paper upon rheumatic angina, recites among others a case (V.) almost precisely like those reported above, except for the fact that the patient had in addition some indefinite articular pains without manifest changes in the joints.

A discussion of the relations of the rheumatic manifestations would, as I have before said, unduly lengthen this paper; I would, however, mention that I have seen, and in a future paper hope to report, one or more instances of the occurrence in the course of or after acute tonsillitis of each of the rheumatic associates, with the solitary exception of subcutaneous fibrous nodules, which are conspicuously rare in this part of the world.

My reason for making this report upon what is really but a small portion of a very large subject, is to again call attention to a grave complication and sequel to a slight primary disorder, and to a pos-

sible factor in the causation of many otherwise unexplainable cases of cardiac lesion, and also to add a small contribution to our knowledge of the etiology of acute articular rheumatism.

DISCUSSION.

DR. TYSON: Endocarditis is not the only disease which is a manifestation of a certain degree of virulence in what is commonly known as simple tonsillitis. It happens to me a couple of times every winter to have brought to me cases of nephritis that originate apparently from this form of tonsillitis. Whether or not the throats of these cases would exhibit any micro-organism on bacteriological examination I do not know, but I am quite sure that this causal relation does exist between the simpler forms of tonsillitis and nephritis. Endocarditis or nephritis may originate from septic matter either generated by or associated with this tonsillar inflammation.

DR. THAYER: The manner in which an acute tonsillitis may sometimes serve as the point of origin for general infection was brought forcibly to my attention a short time ago by a case which occurred in the practice of a friend. A child had had a slight tonsillitis, which within twenty-four hours after the first symptoms was followed by convulsions. The child became quite unconscious; there was a high fever, some stiffness of the muscles of the neck, and death followed within thirty-six hours. Autopsy showed no gross lesions, but cultures demonstrated a general streptococcus septicæmia.

DR. THOMSON: I recall a case that may be interesting in this connection. The gentleman told me at my first visit that he had been subject to quinsy, and always dreaded the attacks because they were followed by rheumatism. He was at that time suffering with great mental depression on account of serious financial losses, and had a suppurative tonsillitis, which had burst that morning. The next day, at my first visit, he had developed pleurisy, with a soft systolic murmur, which rapidly turned into a harsh murmur, with other signs of endocarditis, and he died on the seventh day, comatose. There can be no question that he had one of those rapidly developing cases of endocarditis, the connection with tonsillitis being about as close as any two events occurring together can be.

DR. DOCK: I have occasionally made observations so similar to these that I have come to believe, in recent years, that many so-called rheumatisms are manifestations of various kinds of infection, often septic. I wish to mention now only a single case which I have had under observation for some time a previously healthy woman, who has a so-called rheumatic iritis. The real

nature of this is, of course, obscure, but the common name indicates a prevalent view. She had subacute rheumatic joint symptoms, swelling, with high temperature, and the pain was relieved by the salicylates in the usual way. The only cause that could be discovered for the infection was a severe sore-throat two weeks before the eye-symptoms began. The sore-throat was followed by rheumatic pains such as are seen in some cases of influenza, and thought by the patient to be that disease. The eye-symptoms then came on, with those in the joints later. The case struck me at the time as a striking example of the kind Dr. Packard has brought before us.

DR. PACKARD: I grant that in three of my cases I could not say positively whether the heart was normal before the attack of tonsillitis, although there was no evidence to the contrary. In two I had examined the heart frequently before, and know that, so far as physical signs can tell us, there was no lesion of the endocardium. The point that I wished particularly to make was that we ought to cease speaking of endocarditis, tonsillitis, etc , as being rheumatic. I believe they are infections, or the results of infection. The point of entrance is usually at the tonsils or pharynx, and the poison so entering may affect the endocardium as well as other structures.

A CASE OF FATAL EPISTAXIS (FROM ENDOTHELIOMA OF THE NOSE), WITH A STUDY OF THE BLOOD.

By GEORGE DOCK, M.D.,
OF ANN ARBOR.

G., aged thirty-seven years, hotel-keeper, was admitted to the University Hospital, January 10, 1899, on account of a severe nose-bleed.

His father died at eighty-nine years—cause unknown—his mother at fifty-two. She had a "rose cancer" over the pubes, which was removed. One brother is living at forty-five years, and one sister at forty-seven; both well. There has been no history of excessive bleeding in the family. Has one boy, thirteen years old; well.

G. was well as a child. Has had whooping-cough, measles, and mumps, with no sequelæ. No history of venereal disease. Smokes, and drinks whiskey in moderation.

Last August had hay fever (had had attacks for past three years), which became better after the first frost. Since then has had "catarrh." Five weeks ago his nose began to bleed; it bled for four hours, "filling a wash-basin." A week afterward there was another attack, which lasted three hours; two days later another, lasting two hours; another, three days later, lasted three hours; next day there was one lasting four hours. He then remained free from hemorrhage for ten days, when he had a severe attack, bleeding three hours. On January 8th bleeding began in the right nostril. This nostril now bleeds whenever the plug is removed, but, with two exceptions, the bleeding was always stopped by plugging. At present, January 11th, there is oozing of blood into the posterior nares, running down into the mouth.

January 12. Patient is very pale and weak; is very nervous; mind clear; both nostrils are plugged; there is marked *fetor ex ore.*

Height, 5 feet 9 inches; weight, one month ago, 218 pounds. Frame very large, musculature moderately developed, soft; panniculus very thick, especially over abdomen. Skin very pale, with slight yellow cast; lips, pale; tongue, pale and dry; there is no icterus; no œdema; joints normal; no enlarged glands.

Thorax: Very large, broad, and deep. Breathing symmetrical. Physical examination of lungs negative.

Heart: Percussion unsatisfactory, on account of thick panniculus. There is a harsh, blowing systolic murmur in the pulmonary area, becoming softer, but audible, over other parts of the region.

Pulse: 120, soft, dicrotic.

Abdomen: Above level of ribs, pendulous. Large amount of fat makes examination difficult. Appetite fair; bowels constipated.

Blood: Thin and watery; red corpuscles, 1,120,000; leucocytes, 13,300; hæmoglobin (Fleischl), 25 per cent.

The urine contains neither albumin nor sugar.

14*th*. Examination of the eyes (Dr. Johnson): There are numerous retinal hemorrhages; several large ones, besides a general diapedesis from the sides of the arteries; great pallor of the eye-grounds.

The patient was treated locally in the throat and nose clinic, having been referred to the medical clinic for the blood-examination. As it was considered probable the blood-condition was the result rather than the cause of the bleeding, no change was made. The treatment consisted in the use of gelatin solution subcutaneously and in the nostrils, subsulphate of iron internally, and on several occasions, when the bleeding was profuse, plugging the nares.

The condition of the blood will be described in detail below.

The patient gradually became weaker, and had repeated hemorrhages, usually moderate, but more or less constant; leaking of blood from the nares when not plugged. Slight general œdema developed. Ecchymoses appeared in a few places on the skin. On January 24th slight icterus appeared, shown most plainly in the urine and scleræ, as the skin was yellowish on admission. On January 25th diarrhœa began, with tenesmus and frequent watery stools. On the 27th œdema of the lungs developed, the pulse became impalpable, and the patient died with increasing dyspnœa.

The *autopsy* was made an hour after death. I give here an abstract from the protocol of Dr. A. S. Warthin:

Anatomical diagnosis: Endothelioma carcinomatosum of turbinated bones; secondary anæmia; fatty infiltration of the liver with lymphoid infiltration; hyperplasia of spleen; fatty degeneration and liquefaction necrosis of heart-muscle with hemorrhages and lymphoid infiltration; broncho-pneumonia and œdema of the lungs; adenoma of prostate; simple hyperplasia of pancreas; arterio-sclerosis; slight icterus.

There is slight hypostatic congestion of the skin; skin and mucous membranes and scleræ pale-yellow; there is an ecchymosis the size of the hand on the right leg; also a small ecchymosis on the left arm. Panniculus very thick. Muscles brownish-red, large. All the tissues are very anæmic.

Examination of the skull and brain negative.

Diaphragm in the normal position. The left pleural cavity contains 300 c.c., the right 400 c.c., of cloudy fluid. The pericardium contains 400 c.c. of slightly brownish cloudy fluid. The membranes are smooth and shining, with numerous subserous hemorrhages.

The heart is large; weighs 694 grammes. All the chambers contain a great deal of thin fluid blood. There are numerous hemorrhages under the endocardium. The subpericardial fat is increased. The right auricle and ventricle contain pale ante-mortem clots. The tricuspid orifice admits three fingers. The left ventricle contains a small, pale ante-mortem clot and a small currant-jelly clot. The mitral orifice admits two fingers. There is a slight thickening of the mitral flaps. Otherwise the valves are negative.

The aorta shows moderate arterio-sclerosis.

The left lung contains air throughout, but exudes a turbid fluid from the cut surface. The right lung shows in the middle of the lower lobe an airless, dense, dark-red area of about 2½ cm. in diameter; otherwise as the left.

The peritoneal cavity contains 200 c.c. of clear fluid. The omentum is very fat.

The spleen weighs 590 grammes. The capsule is tense, not thickened; the cut surface moderately red, slightly granular. Consistency firm, follicles enlarged, stroma increased.

The adrenals are negative. The left kidney weighs 199 grammes. The fatty capsule is excessive; the fibrous capsule not adherent, very smooth; the cut surface smooth, very pale; the glomeruli not dis-

tinct. The right kidney weighs 193 grammes; otherwise as the left. The ureters are negative. The bladder contains a large quantity of bile-colored urine; the mucosa is pale and thin, and shows small hemorrhages.

The stomach contains 400 c.c. of sour, grayish fluid, containing milk-curds. The mucosa is pale and appears atrophic. Small intestine and appendix negative. The rectum contains six or seven small ulcers covered with dirty-gray exudate.

The liver is much enlarged; weighs 3171 grammes. The surface is brownish-red; a flat furrow corresponds to edge of the ribs. Cut surface pale-yellow, very œdematous, greasy; consistency slightly increased. Lobules not distinct. Gall-bladder contains a small quantity of fluid bile.

The pancreas is large and pale.

The retroperitoneal and mesenteric glands are enlarged. All the vessels in the abdominal cavity show moderate arterio-sclerosis. The ribs, sternum, clavicle, skull-cap, and both humeri show no increase of red marrow. Both tibiæ when split show fatty marrow, gelatinous, with very small, scattered areas of lymphoid marrow of pale-pink color.

The peripheral vessels show moderate arterio-sclerosis.

Over both lower turbinated bones are small, soft, jelly-like growths, removed by curetting, as more extensive operation was not permitted.

These small tumors, which could not be detected during life, gave an explanation of the cause of the hemorrhage, and the other changes found are such as might easily be explained by the severe and repeated loss of blood. This was made more certain by the examination of the tissues, which were hardened in various ways, embedded, sectioned, and stained according to different methods.

Microscopic examination. Fatty degeneration and œdema occurred in all the organs to a greater or less degree. The serous membranes, especially in the heart, are the seats of hemorrhages, sometimes of considerable extent.

The growths from the turbinated bones show small alveoli filled with small cells having relatively little protoplasm, lying in a scanty, soft stroma. Secondary growths could not be found with certainty. In the heart, cells lying in rows occasionally suggest the nests of

the alveolar growth, but the same appearance might more readily be caused by the accidental arrangement of blood-cells between the muscle-fibres.

The heart, besides very extensive œdema and fatty infiltration and degeneration, and the subserous hemorrhages, shows a few small areas of small-celled infiltration, usually around vessels.

The liver is the seat of extensive fatty degeneration, especially in the inner parts of the lobules. The portal connective tissue is but slightly increased, but in most cases contains large numbers of small cells. There are also numerous foci of lymphoid tissue, in some cases growing centrally, with sharp outlines, and compression of the adjacent liver-cells, but usually diffuse, extending out in different directions and containing more or less well-preserved liver-cells in the peripheral areas. These areas reach or exceed the size of a single acinus. The capillaries are in many places dilated and contain blood like that obtained from the finger during life, but especially nucleated red corpuscles of all sizes. The well-preserved liver-cells on the periphery of the acini contain a large amount of brownish-yellow pigment, which gives the iron reaction with potassium ferrocyanide and hydrochloric acid. The lymphoid areas have a distinct, rather large meshed reticulum. They contain large numbers of large eosinophile cells with a single round or oval nucleus, a few eosinophile cells with irregular nuclei, leucocytes of various kinds, mostly mononuclear, and nucleated red corpuscles of various sizes. The appearance of these areas is not unlike that of bone-marrow in cases of mixed-celled leukæmia, but the number of eosinophile cells is even greater than is common in such bone-marrow.

The kidneys show slight thickening in the walls of the arteries. A few glomeruli are partly or wholly fibroid. The epithelium is well preserved for the most part. The convoluted tubules are slightly dilated. There are very few areas of lymphoid infiltration, irregular in outline, diffuse, containing large numbers of eosinophile cells and other leucocytes.

The spleen shows an increase of lymphoid cells in the parenchyma. In the latter the capillaries are often wide, and there are large numbers of eosinophile cells, mostly large and mononucleated, nucleated red corpuscles, and large mononuclear leucocytes.

The lymph-glands show chronic hyperplasia. The sinuses are

distinct, contain large numbers of epithelioid cells, but there is no excess of the eosinophile and nucleated red corpuscles.

In the bone-marrow sections from the small lymphoid area show much of the original fat, with small islands irregular in size and outline. These contain large numbers of eosinophile cells, largely mononuclear, mononuclear cells of various sizes with neutrophile granules, nucleated red corpuscles of all sizes, small numbers of cells of the types of lymphocytes and polynuclear cells, and a few polynuclear giant-cells. These lie in a reticulum, and at times in capillaries or larger thin-walled vessels.

Cover-glass preparations from the lymphoid marrow show many nucleated red corpuscles of all sizes and free nuclei, small and deeply staining. The nuclei in the red cells are rather more irregular than in the peripheral blood and have a looser arrangement of the chromatin; the protoplasm rarely shows polychromatophilia. The leucocytes in these preparations show no variations from those common in red marrow.

In order to interpret the changes described we must consider more in detail the phenomena observed in the blood during life.

After admission the red corpuscles fell considerably and reached the minimum a week after (January 20th), with red corpuscles, 357,600; Fleischl, 20 per cent. The next day, however, the red corpuscles rose to 820,000, and remained about the same, falling to 760,000 two days before death. The leucocytes, moderately increased (13,300) on admission, numbered 30,500 on the 17th, 49,656 on the 20th, 48,000 the 21st, and 35,000 the 25th. The blood was examined microscopically daily, and differential counts of the leucocytes and the nucleated reds made almost daily. It was difficult to estimate the leucocytes accurately in the hæmacytometer on account of the confusion with nucleated red corpuscles, and there is a considerable error for that reason, but one that in the case of the leucocytes is not of material importance. It would have been better to have counted all nucleated cells in the blood-counter and then to have made out the proportion of white to red in dried preparations. In this, however, there would still have been the possibility of error from the overlooking of the smaller nuclei in the blood-counter.

The leucocytes show slight but interesting anomalies.

The small lymphocytes varied at times, but were never excessive.

On January 12th there were 6.2 per cent.; 16th, 2.1; 19th, 2.7; 22d, 6.9; 25th, 7.9.

The large lymphocytes—*i. e.*, those larger than average red cells, and with paler nuclei and more protoplasm than the preceding—numbered: January 12th, 21.4 per cent.; 16th, 14.1; 19th, 27.2; 22d, 25.7; 25th, 23.5.

The polynuclear (neutrophile) cells, varying more in size than normal, but otherwise not remarkable, numbered on the same days: 67.3, 69, 60.1, 54, and 57.2 per cent.

The polynuclear eosinophile cells formed on the respective days: 2.6, 2.5, 3.3, 2.3, and 1.8 per cent. They presented no peculiarities of structure, though varying in size among themselves, and were rarely degenerated. Mononuclear eosinophile cells were always present, but often not numerous enough to appear within the ca. 1000 leucocytes counted. Twice (January 12th and 22d) they reached 3 per 1000 and once (25th) 4. They were usually large, with round or oval nuclei.

Cells with basophile granulations (methylene-blue) were always present to the extent of about 1 per cent.

Myelocytes (of Ehrlich) were always present, but not very numerous—0.3 to 3 per cent.—up to the week before death. They then reached 9.7 per cent., and amounted to 7 per cent. the day before the last. They showed characteristic staining properties and varied considerably in size.

Degenerated cells, usually only the nuclei, polymorphous, or round, were present to the extent of about 1.5 per cent.

On the whole, the leucocytes show simply a total increase of all forms, with such abnormal varieties as occur from an excess from different causes. No example of mitosis was found among these cells.

The red corpuscles present more interesting features. In size they are, for the most part, normal or slightly below (about 7 μ measured dry), but there are a few large ones, up to 10 μ, and a few small ones. Very small cells, such as occur in pernicious anæmia, are extremely rare. Poikilocytes are not numerous, but evidences of protoplasmic degeneration, such as fissures, vacuoles, and coarse granular appearance, are not uncommon.

Variations in the staining of the red corpuscles are also frequent. Shadows, not taking any stain at all, are occasionally found, and

between them and cells taking a normal stain are all varieties. Polychromatophilia in the non-nucleated cells is also occasionally seen.

The most important feature in the blood is the enormous number of nucleated red corpuscles. Considering the source of error mentioned above, there were on admission from 2370 to 2840 per c.mm. —that is, if only leucocytes were counted as such, there were 2840 nucleated red corpuscles per c.mm—if all the nucleated reds were counted as leucocytes, there were 2370 nucleated reds per c.mm. The real number lies between the two. In five days, with a leucocyte count of 30,500, the proportion was even higher—21 instead of 18 per cent.—so that the maximum count of nucleated reds on that day would be 7320, the minimum 6543. With the maximum leucocyte count of 49,656, the proportion of nucleated reds to all nucleated cells was 37 per cent. This would give 18,372 red corpuscles; but if the reds were all excluded in the leucocyte count there would be at that time 26,391 nucleated reds. At the last count, with 35,000 leucocytes, there were 33 per cent. of nucleated reds, or 11,555, with a maximum of 17,712. Even the minimum figures show a very unusual condition. I have once before seen nucleated red corpuscles in the same relative proportion to leucocytes, but in that case there was a low leucocyte count. Von Noorden, in the case in which he first noticed the now well-known blood crisis, counted as many as seven nucleated red cells in a field of the oil-immersion lens. In my preparations it is not uncommon to find as many as ten or twelve to a field in a very thinly spread preparation.

A few free nuclei, usually easy to distinguish from the small lymphocytes, are always present. Sometimes these have a very thin hæmoglobin rim.

In size of body the nucleated corpuscles vary from 5 μ to 15 μ. One in mitosis measures 17.5 μ by 13.6 μ. The nuclei show all varieties, from the small, deeply staining and compact form to the pale and large one, often showing a well-marked chromatin network, and those in indirect division. The small nuclei, of normoblast type, are always more numerous, and are most frequently found in cells about the size of normal red cells, though they sometimes occur in much larger ones. Irregular nuclei, in trefoil, or ace of clubs, or rosette figures, are numerous; often the nuclei are near or overlap the edges, and in many

cells the nuclei are broken into numerous irregular bits, and in some cases the escaping nucleus has a distinct rim of hæmoglobin.

Measuring and counting 500 successive nucleated red cells (January 19th) I found 48 over 10 μ in diameter. Fifteen of them had small, compact, or lobulated nuclei. The other 33 had nuclei of the typical megaloblast type. These are relatively large, round, or elliptical, often eccentric, but never protruding from the body, with the chromatin in a more or less distinct meshwork, in which the nodal points are often well marked. Cells having nuclei of this type, but less than 10 μ in diameter, are common. Out of the above 500, 23 were of this variety.

Mitotic figures can be found in the red corpuscles in all preparations, and in some one can find four to six in a single cover-glass. I allude only to distinct karyokinetic figures. There are always cells with the chromatin in granules or rods, or in a mass suggesting an equatorial plate, but these I have not counted as mitoses. Those found are almost all in the later stages, with disasters, and sometimes beginning division of the protoplasm. Very often two nucleated cells may be seen close together, suggesting recent division; but this is likely to be accidental, as one can also find groups of three, four, or even more, side by side.

The large number of nucleated red corpuscles in this case enabled me to confirm an observation I made several years ago—viz., that the nuclei of the red cells undergo changes of size and shape in the fresh drop under the cover-glass. When I first saw this I supposed it was an optical illusion from the movement of the nucleus out of focus, but careful observation proved this not to be the case. The process was always seen in the small nuclei in rather large cells It consists in a slow, at times rather rhythmical, contraction and expansion, with changes from round to oval and back to round, and change in position in the corpuscle. The various changes can be seen within two or three minutes. That such changes occur has long been known to histologists. It does not seem, however, they are taken into account in discussions regarding the size and structure of nuclei. Differences in the appearance of the larger nuclei also occur in the fresh drop, but I did not have time nor opportunity to watch the corpuscles long enough to see the process of indirect cell division, as did Askanazy (*Zeitschrift für klin. Med.*, Bd. xxiii. p. 90). I made an effort to

obtain evidence of both processes by keeping freshly spread covers in the moist chamber at 37° C., and fixing them by alcohol and ether at intervals. In preparations made in this way I found that in blood containing a large number of normoblasts the nuclei were on the average larger and showed a more distinct meshwork ten minutes after removal. At fifteen minutes they were smaller again. After twenty minutes the cells began to break down, the nuclei swelled, stained deeply on the periphery and faintly in the centre. Mitosis was not more common in the preparations than in those dried quickly.

The protoplasm of the nucleated cells shows important staining characteristics. In many cases the protoplasm takes a more or less marked blue from hæmatoxylin, either diffuse or in fine meshwork, or very rarely in fine granules. With Ehrlich's triacid stain such cells take a darker color than the rule. Some of these cells are evidently erythroblasts of Löwit. Polychromatophilia is most commonly found in the megaloblasts of all sizes, but also occurs in cells of true normoblast type. In many dividing cells, and in some with very large nuclei and narrow protoplasm, the latter takes a uniform pale-blue color with hæmatoxylin, not unlike that in certain leucocytes, and, in in fact, many of the cells with indirect nuclear division closely resemble dividing myelocytes. I have never, however, found the nuclei in the blood-cells in the present case precisely like those in myelocytes as one sees them in leukæmic blood and in bone-marrow.

In a few cells there is a sharp demarcation, sometimes even a fissure, separating the part of the protoplasm that takes the basic stain from the inner acidophile part.

In the interpretation of the case the most obvious fact appears to be that the striking changes found in the liver, spleen, and bone-marrow are closely connected with regeneration of the blood following hemorrhage. Neither the nasal tumor nor its secondary results can directly account for these.

The important features about the changes are that those in the bone-marrow are relatively slight, those in the spleen, as usual, difficult to determine, and those in the liver unusual and striking. I do not know of a similar observation. It is noteworthy that the capillaries of the liver, on the whole, do not present such marked evidence of blood formation there as is seen in many anæmic diseases, but the process occupies large foci.

The case also illustrates the practical impossibility of making a sharp distinction between normoblasts and megaloblasts, and strengthens the opinion I have formed from other cases, that a morphological difference does not exist, agreeing thus with the views of Askanazy, Schaumann, and Dunin. The convenience of the term megaloblast, however, is undeniable, and the occurrence of transitions to normoblasts only adds to the interests of the former bodies.

To the question whether the megaloblasts are young or old cells—still an open one—I think the answer must be that they are young. This view is based on the structure of the nucleus, and on the frequency of mitoses in these cells. So far as the polychromatophilia is concerned, this is no doubt often an evidence of degeneration, but as Gabritscheowsky has well remarked, degeneration would be likely to affect young and unformed cells.

Those who share Ehrlich's view as to the nature and significance of megaloblasts will no doubt look on the fatal outcome in this case as proof of their theory. It certainly is a most remarkable fact, that in spite of the extent of blood formation the actual renewal of the patient's blood did not take place, and, although it is hardly safe to draw sweeping conclusions from the case, one is almost forced to believe that, notwithstanding the morphological relationship of the cells, there is a connection between the megaloblastic alteration of the blood-forming organs and the failure to produce good blood. The causes and nature of the change remain as most important and interesting problems.

DISCUSSION.

DR. THAYER: I saw about six years ago a case that in certain respects bore some resemblance to that described by Dr. Dock. It was a case of fatal anæmia in a man between fifty and sixty years of age, where the blood showed enormous numbers of nucleated red corpuscles, apparently as many as in this case. They differed, however, in character, in that they were all of small size, with small, deeply staining nuclei; there were absolutely no megaloblasts. In that case there was a progressive anæmia, ending fatally. There was a great excess of small mononuclear leucocytes. The leucocytes were increased in number, at one time reaching as high a figure as 80,000 to the cubic millimetre, so that the picture was almost that of a lymphatic

leukæmia. Unquestionably fatal cases of anæmia may occur where the nucleated red blood-corpuscles in the circulating blood are all of a normoblastic type.

DR. STENGEL: In the examinations of the blood of post-hemorrhagic cases that I have made normoblasts and microblasts have been the forms of red corpuscles that were discovered; but I have never seen a case in which there was anything like the number of nucleated red cells that occurred in Dr. Dock's and Dr. Thayer's cases. I agree with Dr. Dock that no sharp line can be drawn between the different types of red corpuscles. They seem to me to be variations which merge into each other without any sharp distinctions. I cannot agree, however, with him, as far as prognosis is concerned, that there is any significance either in the mere presence or the kind of nucleated red corpuscles. Some have gone so far as to say that the diagnosis of pernicious anæmia could not be established in a case in which the microblasts were present in great excess of the megaloblasts, but I am sure that this is not sound teaching. I have myself observed cases of pernicious anæmia in which there were many nucleated red corpuscles, most of them being of small type, and similar instances might be cited from medical literature. The nucleated red corpuscles seemed to me to be evidences of regeneration of the blood, but whether this regeneration is sufficient to preserve life or not must be judged in other ways than by the mere inspection of the blood.

DR. OSLER: I would like to mention a very remarkable form of epistaxis and to ask the members present if they have had any experience with it. I have had three instances of it developing in early manhood, proving nearly fatal, and associated with the most remarkable development of angiomata over the surface of the skin. Two of these cases were in brothers, and one case died recently of cancer of the stomach, and showed these remarkably large veins from which the bleeding had occurred in the nose. The picture presented by one of the cases was peculiar in that as you looked at him across the room you would think he had a case of acne. I could find no reference to such a condition in literature, and it was interesting to note the association between the varices of the mucous membrane of the nose and the cutaneous angioma.

SUCCESSFUL USE OF THYROID EXTRACT IN THE TREATMENT OF A CEREBRAL NEOPLASM.

By STARLING LOVING, M.D.,
OF COLUMBUS, OHIO.

THOMAS W., aged eighteen years, a student. Of medium height, well-developed, with a decided tendency to corpulency. Weight, 170 pounds; skin fair, but thick and of an unhealthy, sodden appearance; brown hair; blue or gray eyes, pupils large and sluggish; regular but smallish features; expression of face dull and lacking in intelligence; speech shows mental movements slow but coherent. Locomotion slow and uncertain, as though the muscular system is weak; the influence of the will imperfect and the vision impaired; but there is no paralysis. Pulse 72, soft and regular; temperature normal. Cutaneous sensibility unimpaired; reflexes rather tardy, but otherwise intact. Functions of the alimentary organs normal, excepting a tendency to constipation. Respiratory and circulatory organs normal. Urine of normal quantity and negative to tests.

Family history good, and without trace of tuberculosis, syphilis, cancer, alcoholism, or nervous disorder. Personal history also good. In early childhood he had chickenpox and measles, and four years ago an attack which his physician called typho-malarial fever, but does not remember to have had any other illness until late in the year 1895, when, while in the pursuit of his studies, without assignable cause, he began to suffer from frequently recurring attacks of headache, accompanied on one or two occasions, when he had eaten immoderately, with nausea and vomiting. Except on those occasions, however, even when the pain is most intense, his stomach is not disturbed.

In the course of three months, the headache continuing, he found that his vision was failing—*i.e.*, he could not distinguish figures and

drawings on the blackboard, nor the print in his books clearly, nor was he able to write legibly. The failure of vision was not attended with pain or other disturbance of the eyes. The headache at length became almost constant, with frequent exacerbations, especially after unusual exertion. It was, and is now, often so severe at night as to disturb sleep. The impairment of vision increased with the severity of the headache, and in June, 1896, he was obliged to abandon his studies and seek medical advice.

He consulted several physicians, among them Drs. C. S. Hamilton, C. F. Clarke, W. K. Rodgers, and A. B. Richardson, all of whom, from the duration and intensity of the pain, sometimes frontal, sometimes occipital, but generally diffused over the entire head (the patient said "right in the centre"), with the impairment of vision, without corresponding lesion of the retina or other ocular tissue, arrived at the conclusion that there was an intracranial growth, the nature and precise location of which they were unable to determine. After consultation, and by the advice of Dr. Richardson, the patient was ordered an alterative course of treatment—that is, he was given green iodide of mercury and iodide of potassium—which, after a fair trial, yielding nugatory results, was abandoned, and the patient was referred by Dr. Clarke, October 15, 1896, to me for examination and what I might consider appropriate treatment.

I was unable to make an entirely satisfactory diagnosis, but, from the history and symptoms, concluded with my friends that there was an intracranial progressive neoplasm, the nature and precise location of which were somewhat conjectural.

The history and present condition of the patient precluded tubercular infection; from extreme rarity the growth could hardly be parasitic; the progress of the malady had been rather slower than that of glioma, sarcoma or syphilis, but it might be one or other of the three last named.

From the character of the pain and the impairment of vision without adequate ocular lesion, I was inclined to think the growth was situated in the middle fossa.

Hoping I had a syphilitic case, though aware that the young man had already been treated with mercurials and potassium iodide, I determined to further test the effects of those remedies. Accordingly, after directing moderate out-door exercise, plain but substantial diet,

and a nightly warm bath, prescribed corrosive sublimate, dissolved in compound tincture of cinchona, internally, with gray ointment by inunction, and continued the course until the gums became swollen and the mercurial fetor unmistakable, without, however, the slightest improvement in the patient's condition. The mercurials were, of course, suspended, and after ten days, when the mouth had healed, the potassium iodide was given internally, in doses of twenty grains, dissolved in a mixture of hot water and milk, before each meal, and the ointment applied externally to armpits and groins.

After fifteen days there were decided symptoms of iodism, with irritation of the stomach, greatly impaired appetite, and loss of flesh, and again without diminution of the pain or improvement of vision. Patient was despondent.

It was quite apparent that the case was not of syphilitic origin, that no benefit was to be hoped from mercury or iodine, and that all perturbative treatment should be suspended until irritation of the stomach had subsided.

Prescribed infusion of wild-cherry bark, and, after a few days, when the irritation of the stomach had subsided, in order to stimulate the appetite more decidedly, substituted quinine with citrate of iron. Food and baths as before.

January 17, 1897. The patient has regained his appetite and former strength, and, in a measure, his spirits, but there is no diminution of pain nor improvement of vision. He is exceedingly anxious to recover, and begs that radical treatment of some kind be resumed.

I now suspected glioma, and reasoning from its influence in myxœdema, goitre, obesity, and, as reported by Dr. Kinnicutt and others, in some other affections—remembering its chemical relation to iodine and with the characteristics of the gliomata in mind—prescribed thyroid extract in doses of three grains, one dose to be taken with hot water before each meal, with the hope that as the remedy has such decided effect upon what may be called neoplasms, or at least upon morbid increase of tissue in the maladies above named, it might remove what was most probably a neoplasm in the case under charge.

The medicine was taken regularly in the doses mentioned until February 1st, when the quantity was increased two grains, and continued until March 15th, when there was manifest improvement.

There was much less pain, better vision, a change in the expres-

sion of the face, more natural and brisker bodily movements. Gratifying but not entirely satisfactory progress, and the dose of the extract was increased to six grains, and continued at the same intervals until April 20th, improvement continuing. On May 1st, although there was almost entire subsidence of pain and further improvement of vision, as there was notable loss of flesh (nearly twelve pounds), the remedy was suspended.

On May 12th its administration was resumed in doses of five grains, and continued until June 15th. As the patient then declared he had no more headache, and that he could see very well, medication was suspended, and he was referred back to Drs. Clarke and Rodgers for examination.

The subjoined report, which Dr. Clarke courteously prepared and sent me, conveys accurately the condition of the patient's eyes on October 15, 1896, and proves the change which had occurred in their functions June 27, 1897, the date of the last examination.

August 16, 1896. Thomas Walsh, aged eighteen years; student.

Vision: R. 1/xv —2.s lens improves slightly. L. 1/xL—unimproved by lens.

Ophthalmometer: R. 1.5 ax. 90° (corneal astigmatism). L. 1.75 ax. 90° (corneal astigmatism).

The ophthalmoscope reveals slight dulness of the retina, and in the disk region the veins slightly prominent and tortuous and somewhat contracted. His vision, he states, as does his mother, was formerly good, but the ophthalmoscope does not fully explain the marked depreciation which has taken place. There is some indistinctness of the outlines of the disks, and possibly some atrophy of the grayish order.

His visual fields are good.

Color-sense somewhat defective. He confuses blue and pink. Slightly "red blind."

August 19, 1896. Vision as above.

Ophthalmoscope: I to-day note more pronounced dulness of the disk margins. Tumor of brain suspected.

℞. Pot. iod. gr. xv, three times a day.

August 27, 1896. R. E. — 2.s 1/xv (as above). L. E.—1.5 1/xx, improved slightly.

Ophthalmoscope: As above in disk region.

℞. Hydrarg. protoiod. gr. ⅛ t. i. d.

September 17, 1896. Vision as above.

Ophthalmoscope: As above.

On Dr. Richardson's suggestion he was given protoiodide of mercury, gr. $\frac{1}{5}$ four times a day. No improvement.

October 15, 1896. Referred to Dr. Loving.

June 27, 1897. R. E. 1/v = three times vision when he came (with — 2 c. ax. 180° 1/v +).

L. E. 1/x four times vision when he came (with 1 c. ax. 90° — 2 c. ax. 180° 1/v, which is eight times vision when he came).

Great improvement. In other words, the improvement in vision, which I understand has appeared only since taking thyroid extract, is in the right eye to three times what it was when he began treatment, and in the left eight times.

When the ophthalmic examination had been completed the patient was directed to resume his medicine, a dose of four grains morning and night, until further instructions.

I have not a precise idea how the thyroid extract operated. Its effect was that of the alteratives as defined by one of the best of the older writers on materia medica:

"Alteratives are medicines which, without essentially elevating or depressing the vital actions, nevertheless produce changes in the organization or functions which render them available for remedial purposes. . . . . produce no readily discernible changes in the healthy states, and are only known to possess remedial powers by the result of their use in disease."

Thyroid extract is certainly an alterative in the sense just defined, and, in that in health and disease it increases the rapidity of tissue change often to a great degree, it is something more.

As it is certain that other medicines were vigorously applied with no beneficial but injurious effects, and that improvement became apparent at the end of six weeks, and almost complete recovery had occurred at the end of four months and a half from the time its administration was begun, no other medicine having been used in the meantime, it would appear equally certain that the thyroid extract acted as a curative in the case under consideration.

Excepting loss of weight (twelve and a half pounds) and occasional slight disorder of the stomach, as shown in uneasiness, temporary diminution of appetite, and eructations, the medicine caused no un-

pleasant disturbance, such as prostration, palpitation of the heart, vomiting, and rapid emaciation, not unfrequently observed, especially where there is an idiosyncrasy, or when it is given in very large doses. In my case it conformed in action with the definition of alteratives quoted, and "produced (except in loss of flesh) no readily discernible change in the healthy states."

I have found nothing concerning its use in cases in which the brain alone appeared to be involved, especially when glioma has been suspected, and venture this report in the hope that it may suggest the further investigation and use of the remedy.

April 20, 1899. The patient is now engaged as a copying clerk in the water works department, sees almost perfectly, has had no return of pain, has grown nearly an inch, and seems in perfect health.

PERFORATION OF THE STOMACH IN AN INFANT SEVEN WEEKS OLD.

By T. M. ROTCH, M.D.,
of Boston.

The following case is reported as unusual and of especial interest from a pathological stand-point.

A male infant, aged seven weeks, was admitted to the Infants' Hospital, February 2, 1899. The history given at the time of entrance was that the infant had been well until four days previously, when his abdomen became suddenly much distended and he appeared to suffer considerable pain. After the first twenty-four hours the bowels had moved regularly, and the pain had lessened. Vomiting had begun about eight hours before entering the hospital.

An examination by Dr. Dane, the surgeon-in-charge, and by Dr. Morse showed a well-developed and fairly-nourished infant. The facial expression was rather drawn, the eyes dull, and the abdomen much distended and tympanitic, excepting that there were very slight areas of dulness in both inguinal regions. A few coils of distended intestine could be detected. The pulse was 165, the temperature 101° F., and the respirations 35. The diagnosis of peritonitis was made, and it was decided to operate at once. Ether was given, and an incision four inches long was made in the median line, and about two drachms of slightly flaky serum exuded. The vessels of the much distended small intestine, and especially of the mesentery, were found to be very much injected. A few flakes of lymph were found adhering to the intestines. The intestine was thoroughly examined, practically through its whole extent, without any cause for the peritonitis being discovered. The abdominal cavity was irrigated and the wound closed. Three days later the infant died.

Eighteen hours after death the autopsy was made by the pathologist to the hospital, Dr. W. F. Whitney, to whom I am indebted for the pathological diagnosis and for the sections of the lesion.

The body was that of a well-developed infant; rigor mortis was present.

There was an incised wound about 6 cm. long in the median line of the abdomen just below the umbilicus. This was partly closed at the ends by interrupted sutures, while from the middle projected a wick of gauze. This reached well down to the root of the mesentery, and was surrounded by coils of intestine, which were glued to the abdominal wall and to each other. There was no free fluid in the pocket drained by the wick. The adhesions between the coils of intestine could be easily separated, and lying between them was a little opaque, turbid serum in which were occasional flakes of lymph.

The head was not opened.

The lungs were of normal color, well retracted, with a few dark, slightly depressed areas. The pleural surface was smooth and the cavities normal.

The heart was normal and weighed 65 grammes.

The condition of the lower part of the peritoneal cavity has been previously described. The stomach was quite extensively adherent to the diaphragm along its anterior surface, and on carefully separating the fibrinous adhesions one point was noticed where the exudation was a little thicker and more adherent. Embedded in this, and apparently coming from the wall of the stomach, was a minute thread about 2 or 3 mm. in length. There was also a little more injection than elsewhere in the immediate vicinity of this spot.

On opening the stomach it was found to be generally normal, with the exception of a minute loss of substance surrounded by a reddened zone opposite the place of greatest exudation on the outside.

This portion of the wall of the stomach was cut out, and after hardening in Zenker's fluid was mounted in paraffin and a series of sections cut. As the result of the study of these it appeared that there was an oblique passage from within outward through the entire thickness of the wall, and in it lay a foreign body. This was made up of a bundle of very small, irregularly rounded, structureless fibres, staining intensely with aniline dyes, but not with hæmatoxylin.

The edges of the mucosa were slightly rounded over from within

FIG. 1.

Normal size.

FIG. 2.

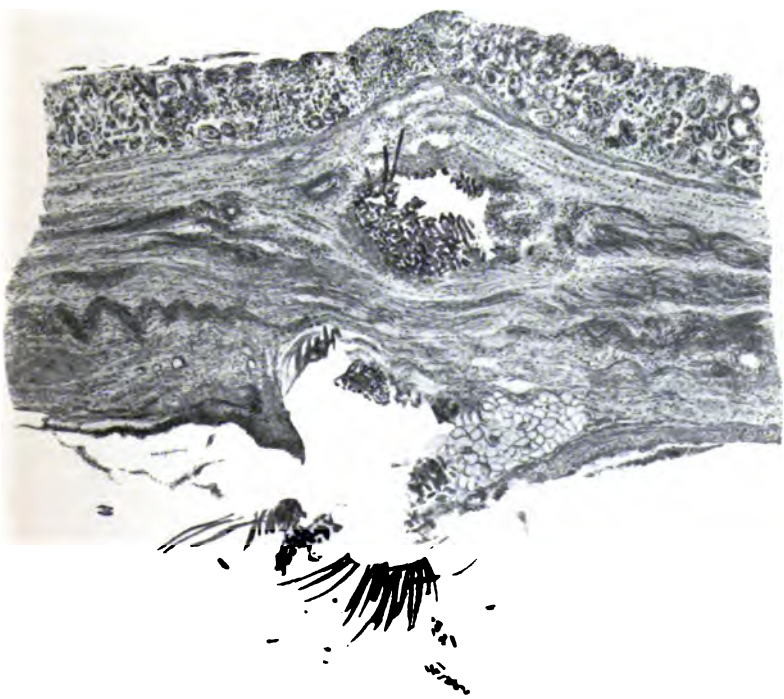
Normal size.

ROTCH—PERFORATION OF THE STOMACH IN AN INFANT.

FIG. 3.

Microscopical section.

FIG. 4.



Microscopical section.

ROTCH—PERFORATION OF THE STOMACH IN AN INFANT.

outward, as if the original lesion had been in that direction. The cavity in the middle coat was partly filled with leucocytes and round cells surrounding the fibres, but not infiltrating among them, and nowhere did the foreign body project into the interior of the stomach.

After staining by Gram's method, large numbers of small rod and spherical bacteria were found on the peritoneal surface close to the thread. No cultures were taken at the autopsy, on account of the lapse of time after death.

The liver was normal in appearance and weighed 165 grammes.

The kidneys were pale and together weighed 35 grammes.

The spleen was dark red and weighed 15 grammes.

The pancreas, adrenals, and genital organs presented nothing remarkable.

The chief interest in the case centres in the perforation and its cause. That the general peritonitis had started from this point there was little doubt, as the evidences of the inflammation were most extensive here and the exudation thicker and firmer. It is highly improbable that this could have been anything introduced at the time of the operation, for to have produced the lesions would have required several days, as shown by the thinned and somewhat everted mucosa. How the perforation took place from the inside is also hard to understand if this foreign body is nothing but a bit of silk thread, as its structure would indicate. It is suggested that possibly a threaded needle was swallowed, and had perforated, leaving a bit of silk behind, and the needle was overlooked among the coils of intestines. It certainly was not thought of at the time of the autopsy, and no especial search was made for it. Another suggestion is that it was a case of follicular ulceration, and the bit of thread had worked its way into that. But the loss of substance in the mucosa is rather less in extent than deeper in, and there is no evidence of any inflammation in the neighborhood that would warrant the assumption of such a process.

We are left, therefore, with the simple fact that the local lesions are all in the immediate neighborhood of the foreign body, and that the perforation and the secondary fatal peritonitis must be referred to it.

The appearances to the eye and under the microscope are well shown in the accompanying drawings made by Miss Byrnes.

ON TABES.

By M. ALLEN STARR, M.D., Ph.D., LL.D.,
of New York.

The study of degenerative disease in the neuron, as revealed by the recently invented staining-methods of Nisll and Marchi, has forced upon pathologists a modification of older views regarding the origin and nature of sclerotic processes in the spinal cord. It has also thrown light upon the hitherto mysterious limitation of such sclerosis to particular tracts, and has revealed the true nature of the so-called "system-diseases." The view of Weigert, that sclerosis is merely a secondary product of nature, to supply a defect when disease destroys tissue, must be accepted. And in consequence the sclerosis becomes of less interest than the primary degenerative process which precedes it. This primary degeneration appears in many cases to affect one physiological set of neurons only. Thus the motor neurons are attacked by the infective agent, producing infantile spinal palsies. Alcohol attacks both motor and sensory neurons; and in tabes it is the sensory neurons which alone present the features of disease. Hence the sclerosis is confined to the regions through which the affected neurons pass, and in tabes is limited to the area of sensory neurons.

The sensory neurons are of many kinds and have different situations, but it is only two particular sets of these neurons which appear to suffer in tabes—viz., the sensory elements of the optic apparatus in the brain and the sensory elements of the spinal cord, whose primary centres are in the posterior spinal ganglia, and whose double branches extend to the surface of the body in the peripheral nerves and to the medulla oblongata through the posterior columns of the cord. It is true that auditory atrophy and loss of the senses of smell and taste have been recorded as occurring in the course of tabes, and we may

perhaps admit the possibility of every form of sensory neuron being involved in the degenerative process. But such cases are rare, so rare in comparison with the general run that we may consider them the great exception. While, then, in the ordinary disease the spinal and optic neurons seem to be the ones most vulnerable, it is to be noticed that they are by no means uniformly involved together. In three hundred consecutive cases of tabes, optic atrophy was present in thirty only.

Nor are these neurons attacked simultaneously. In twenty-five of the optic atrophy cases blindness was present many years before any other symptoms of tabes, except the loss of knee-jerk, developed. In fact I have long been impressed by the fact that cases of tabes in which optic atrophy is an early symptom rarely presented the typical symptoms or the usual course of ordinary cases of tabes. Thus pains, numbness, incontinence, and ataxia may never develop in these cases, or if they do, may be isolated symptoms and may be insignificant for years. It seems, therefore, entirely justifiable to separate the spinal type of tabes from the optic type of tabes and to consider them both degenerative diseases of the sensory neurons, but not the same disease. In the spinal type it is true that optic atrophy may appear late in the course of the case. In the optic type spinal symptoms may eventually develop; but in their onset, origin, and course these types seem to be as distinct from each other as are the sensory neurons which are the subject of degeneration.

No one can observe a large number of cases of spinal tabes without reaching the conviction that in different cases the course of the disease is so various as to present several different types. This renders the prognosis in the early stage most difficult. Thus some patients will have acute pain, attended by irritability of the bladder, by muscular twitching, and by general defective nutrition. They may emaciate rapidly and develop extreme ataxia within a year. They are subject to many of the multifarious symptoms, they suffer intensely, and they die soon of some complication; and no care in treatment seems to avail to arrest the disease or to mitigate its severity. Other patients, on the contrary, suffer little, or have only occasional attacks of pain, for many years after the physical signs of the disease—the loss of knee-jerk, the loss of pupil action to light, and the swaying in the dark—are well marked. They present few symptoms and none of

the rare complications. These patients sometimes go on for years without showing a true ataxia, and, even if a little unsteady in gait, are perfectly able to go about and conduct their affairs for twenty years after the onset of the disease.

Surely the nature and degree and progress of the degenerative process in these cases must be wholly different, and even if the eventual lesion is the same its development varies. I wish to emphasize these different types of tabes for the purpose of calling attention to the necessity of treating them in a different manner. I believe that the course of the disease can be modified by treatment, and that the result of treatment in various places and by various methods has been of benefit very largely because the element of degeneration has been successfully combated.

I have seen cases which I regarded as hopeless and incurable very materially benefited by certain measures. And I have seen cases which I took to be chronic and slow made rapid and fatal by certain measures. I wish, therefore, to call attention to certain therapeutic considerations in the care of tabetics which I believe will tend to alleviate symptoms, to prolong comfort, and to prevent a rapid course of the disease. It is the pathological point of view which directs to the proper line of treatment. We are treating a degenerated condition.

Of the first importance in any case is the general nutrition of the individual. To build that up is the primary object. This is to be done by generous diet, by moderate stimulation, by every possible means to promote the assimilation of food, such as country-life out-of-doors, moderate exercise just short of the point of fatigue, general massage, and particularly by warm baths, long-continued, never attended by shocks or forcible douches, but accompanied by rubbing. The use of antisyphilitic remedies, often indicated, since at least sixty per cent. and probably seventy per cent. of the patients have had this disease, should be put off until the first object has been attained; for if an anæmic, ill-nourished tabetic is given mercury and potassium iodide with hot baths, as at Arkansas Hot Springs, or Aix-la-Chapelle, he may be rendered infinitely worse. On the contrary, if he is first built up and made robust and red with good blood, the same cure may be of the greatest value, even arresting the progress of the disease for years.

There is at present too great a tendency on the part of some practitioners to resort to very limited methods of diet. I wish to point out the danger of this to tabetics. I have seen patients with gastric and intestinal crises assured that some particular diet directed to their digestive organs would cure them; and I have seen them later, after living on milk alone, or on meat and hot water alone, or on diabetic diet alone, reduced to skeletons and subject to many more symptoms of their disease than they had at first. There is every reason for a tabetic to use any form of food that he can digest and assimilate by natural or by artificial means. There is never a reason for starving him. I think alcohol in such cases is not to be excluded, as in moderation it may help digestion, though in excess it certainly increases the pain and ataxia.

I have been very much impressed by the remarkable improvement which has followed water-treatment in a number of my patients. Some have gone abroad to La Malou, or to Nauheim, or to Baden, or to Luchon. Some have merely taken baths in some one of the now numerous water-cures or hydropathic establishments here or in England. I have rarely failed to see benefit from this method of treatment. Perhaps the course at La Malou may be taken as the best. There the patient sits for one-half to one hour in water of a temperature of 85° to 90°, is then rubbed down and sprayed off with a little cooler water, is never shocked by a forcible douche or by very cold water, is made to lie and rest for an hour after the bath, and is made to spend hours in the open air and sunshine. I imagine that the exact temperature of the water or the exact duration of the bath is really of little moment. What is important is the increased rapidity of the capillary circulation, the increased activity of the metabolic process which is induced by the better supply of blood, and the consequent direct increase in nutrition in the spinal ganglia and in the peripheral nerves secured by these means. The same may be said of massage and its recent exaggeration, osteopathy. It helps a tabetic, in so far as it stimulates the circulation and increases the nerve-nutrition.

A word finally about exercise. The method of Fraenkel, by which skill in co-ordinated movement is acquired by practising certain definite motions by the feet, has been of great benefit to almost every patient who has tried it faithfully. Such patients are too liable to overdo,

and I have seen harm done by too constant practice and by over-exertion in walking. Hence, while exercise is not to be forbidden, it is to be used in moderation. Fraenkel movements should not be done for more than ten minutes in half an hour, and should not be done more than three times in a day, and should always be followed by rest.

So far as medication is concerned, it seems to me that cod-liver oil, the glycerophosphates, arsenic, and all forms of tonics are of more value than any other drugs, since they delay the degenerative process.

The object in the care of tabetics should be to recognize the fact that they carry about with them some poison the influence of which tends to cause a degenerative process in the sensory neurons, and to attempt to counteract the effect of this unknown poison by promoting the general nutrition of these neurons by every means at our disposal.

DISCUSSION.

DR. PUTNAM: I heartily agree with all that Dr. Starr has said, except that I doubt very much if it is not a matter of a great deal of importance just how we use our applications of water. It seems to me that the treatment outlined as that followed at Nauheim would not be indicated in a great majority of cases. The object is to improve the circulation in the deeper-lying organs, and I fancy that there are better means of doing that. These patients cannot stand the shock of very cold water, but they can stand hot water better, and, still better, effects can perhaps be obtained by hot water under pressure which stimulates the sensory nerves of the skin strongly.

As regards the Fraenkel method, I also have found it of value, but I think it is important to have an instructor to carry it on.

DR. SINKLER: I can confirm all that Dr. Starr has said from my own experience. So far as I can recall in thinking over a number of tabetics I have seen, they were all emaciated and anæmic patients. I can only think of one who was not—a man who was in active business for twenty-five years after the onset of the trouble. There is no question that attention to the nutrition is of more importance than anything else. The best results I have seen have followed the removal to a different climate, especially a mild climate like that of Florida or California.

I use the iodides in this disease, but am very unwilling to use the drug, except in very moderate doses, as I have seen disastrous results from large doses.

DR. THOMSON: I am sure that any one with experience in different classes of tabes will agree to their division into an optic and a spinal class One of the first cases I ever had was a man who came to me, having been referred by an oculist, and who became totally blind in a very short time and remained so, but who showed no symptom of ataxia at that time. On the other hand, we may have mixed cases, and I have two of that kind on hand now in which both spinal and optic symptoms are very pronounced.

As regards treatment, I fully concur in what Dr. Starr says of the value of cod-liver oil, and there is not a tabetic that comes to me that is not put upon cod-liver oil. I think well of arsenic also. In certain cases I believe in the use of the actual cautery to the spine. It is so readily done by the patient himself, or by a friend by means of an ordinary small glass tube, the tip heated in an alcohol flame and touched to the spine. I am certain that in a number of cases the symptoms are thus much relieved. Another favorite measure of mine is the red-pepper pack, and it has its uses in dealing with a great variety of symptoms. Sometimes it is applied to the spine only, and sometimes to other portions of the body.

We recognize, too, educational movements, and I can fully endorse what Dr. Starr says of the improvement in the gait in some patients while taking these exercises. I have not yet seen any one injured by them.

As to the baths, I have for the past two years used the artificial Nauheim bath, and it appears to me that the cutaneous impression of the carbonic acid generated there makes them more beneficial than the salts I formerly used. The improvement is such that I believe the prognosis in a number of these spinal cases is a great deal better than we thought of ten or fifteen years ago.

DR. FOLSOM: I was exceedingly interested in Dr. Starr's very interesting paper, and my experience has been much the same. I am inclined to think there is something in the skill with which water is used, and am sure that there is in the skill with which gymnastic exercise is carried out. In regard to the use of the iodides, it seems to me important to begin them as soon as possible, and in my experience I find that the dose the patient will take varies with the individuals. If given two or three hours after meals with Vichy it is an assistance in the building-up process, while I have rarely found it to interfere a bit. My impression is that a larger percentage than sixty or seventy of these cases occurs among syphilitics, though I am not prepared to agree with some writers that tabes is syphilis. The toxic action of the iodides is not so very uncommon, even among patients who have had syphilis, and if the patient begins with a large or moderately large dose of iodide, and some disagreeable effect follows, it seems to me that it is not necessarily a contraindication to the use of iodide in the vast majority of cases. I have had one patient under my care, for instance, in whom iodides seemed to be distinctly indicated for syphilis, and it is quite impossible for him to take it for four days in succession without producing a troublesome œdema of the

retina, and I have another patient who cannot take four doses of ten grains each without it completely closes his eyes. I have also seen some cases of œdema of the brain from this drug. The drug should be watched closely for two or three weeks, but if there is tolerance of it I think it is of service, even in the early building-up process. I have never given the large doses that some physicians give, rarely more than 150 grains a day.

DR. BOND: I wish to emphasize the point brought out by the last speaker as against Dr. Starr, that is, that these patients tolerate the iodides very well. I have two cases under observation now that have gradually improved in weight under the influence of 50 grains of the iodide of potassium daily. I believe, however, that the best way would be to give the iodide of potassium for a week at a time and then withdraw it for a few days in those cases that do not bear it well.

DR. SACHS: I wish to be permitted to say that those of us who have had the opportunity to watch many cases of this disease will quite approve of Dr. Starr's subdivision of the cases. I can fully concur in almost every point he has made in regard to this distinction, and only wish to remark that I was struck by the fact that the amaurotic or optic type seemed, on the whole, to be less progressive than the spinal type.

Before we enter upon the condemnation of the mercurial and iodide treatment, if such condemnation was intended, I think it well to throw out a warning that some cases diagnosticated as posterior spinal sclerosis may be spinal lues simulating tabes. I base that upon a number of observations, and in those cases active treatment by iodides and mercurials is attended by excellent results. While it is unquestionably true that in the later stages of tabes dorsalis large doses of the iodide may do harm, in the early stages I think it is well worth while to push it vigorously.

DR. CARY: I hardly think it is necessary to refer to this point, but it may not be inappropriate to throw out a suggestion in the line of one made here a while ago as to the time at which the iodide should be given. The majority of physicians probably give the iodide upon a full stomach. I think that is a common practice, whereas, as a point of fact, the iodide of potassium should be given without any liability of its coming into contact with starches, and should, therefore, be given one or two hours after meals. In that way the nutrition is maintained.

DR. JANEWAY: Last year I spoke on the subject of chronic syphilitic fever and the use of the mixed treatment in its removal, mentioning six cases. In that treatment I used very moderate doses of the iodide, from five to ten grains, with from one thirty-second to one-twentieth of a grain of mercuric iodide combined with tincture of cinchona. These cases all recovered, and since then I have seen a case of fever of the same kind with

tabes of the earlier stage, so that I had to say the probabilities are here is a fever syphilitic in origin with tabetic manifestations, and upon the same plan of mixed treatment a marked gain in weight occurred. Sometimes I have thought I have overdone it in the amount of iodide used, and I have been surprised to see how in these cases the relief was brought about by the employment of moderate doses.

DR. FOLSOM: I think that the dose has got to be judged for the individual, as a moderate dose to one is an immoderate dose to another, keeping it up sometimes for two or three years, or even longer, with intermissions.

DR. STARR: As to the question of water-treatment, I consider it a very important thing to be precise in one's methods, but some of the best results come from the use of forcible douches and from the alternation of hot and cold water, and these methods being quite prevalent in the treatment of neurasthenia, are apt to be used indiscriminately, and in tabes my warning was against these methods. I believe in the water treatment, with a considerable degree of warmth to the surface, or by slight counter-irritation, such as is produced by the red-pepper pack. The first degeneration appears in the periphery and very often in tabes, even in the middle stage, one finds no actual lesion in the spinal ganglion itself, as Ewing has shown, but you do find distinct degeneration in the periphery of the neuron, both in its distribution in the skin and in the spinal cord, therefore measures directed to the skin are just as likely to increase the nutrition of the neuron as if directed to the spinal cord itself.

I have been misunderstood in regard to my statement concerning the use of antisyphilitic treatment. My paper reads that such treatment is indicated because sixty or seventy per cent. of the patients have had this disease, but that the iodides should be put off until the patient is somewhat built up. I believe that the collection of statistics to prove that all cases are syphilitic has led to a wrong line of treatment, because the majority of doctors who hear that tabes is a syphilitic disease will immediately put their patients upon antisyphilitic treatment, and I want to warn against its use in that way. As a matter of fact, the patients who have had syphilis or show the effects of it should at some time be put through inunctions of mercury and the use of iodide, and I admit I am in favor of large doses, 150 or 200 grains a day; but I believe these patients are not benefited by such a line of treatment until the general health is built up.

ON ASTASIA-ABASIA, WITH A CASE.

By J. C. WILSON, M.D.,
OF PHILADELPHIA.

It is a remarkable fact that the syndrome astasia-abasia has attracted so little attention in America. The earliest account of the condition, according to Knapp,* was given by Jaccoud in 1864. Weir Mitchell, in 1881, reported a case under the heading "Hysterical Motor Ataxia." Knapp's very complete paper was published in 1891. Up to that time he had been able to collect only forty-nine cases, in addition to his own, which presented "some of the symptoms of abasia, but which is not wholly typical." Of these cases thirty had been reported by French observers, and only four had been studied in this country. These were: 1. The case of Weir Mitchell, already referred to (1881). 2. That of Hughes (1890). 3. That of Hammond (1891). 4. That of Knapp (1898). Dr. Kalteyer has been good enough to look up for me the references to this curious and rare nervous disturbance since the date of Knapp's paper. He finds in the *Index Medicus* forty-three separate titles. Of these communications twenty-two are by French or Belgian and five by American physicians. The American papers are those of: 1. M. Prince (1892); 2. Bremer (1893); 3. F. R. Smith (1894); 4. Eshner (1896); 5. Diller (1896). To the nine cases hitherto reported by American observers I desire to add one recently observed in private practice.

A woman, aged twenty-four years, of good position and in comfortable circumstances, is the subject of the following note: She comes of distinguished stock, but on the paternal side there is an uncle epileptic and an aunt addicted to morphine; on the maternal, two uncles dipsomaniacs. Her father was very successful in business, had grandiose ideas, and lost a large

* Journal of Nervous and Mental Disease, New York, November, 1891, xvii. No. 11.

fortune. He is now greatly absorbed in tracing genealogies. Her mother died of diphtheria. She had a sister who died of diphtheria at an early age, and one older than she who is in excellent health, but excitable.

The patient had the diseases of childhood severely, but grew up in good health. She has for some years, since the death of her mother, kept house for her father, who is much preoccupied, but she has had her own friends, and is very intelligent and cheerful. Lately there was an unsatisfactory love affair. Up to this time her health has been excellent. Early in January she began to suffer from bath pruritus. January 16, being at the close of menstruation, she was roused from sleep at midnight by a ring at the bell. She hurried into her wrapper and slippers and opened the door, to receive an indifferent telegram from a member of the family in another city. The next day, on attempting to rise, she found it impossible to stand or walk. With the assistance of her maid she could cross the room, but unsupported she sank to the floor. She described her condition in the following terms: "My left leg feels as though it were made of cotton"—an expression already recorded—and "I feel like a combination of a child learning to walk and a drunken woman." Her people were greatly alarmed, but she treated the matter lightly. In the course of a day or two the following clinical data were collected:

The patient stated, referring to her matrimonial engagement, which had been broken off, that for some months prior to the attack she had been worried. She was slightly paler than usual, but refused to have a blood examination. She had menstruated regularly and without pain. Appetite fair; digestion satisfactory; bowels slightly constipated; up to this time vomiting had not occurred. There were no signs of visceral disease. The urine is normal. Lying in bed or seated upon a chair, the lower extremities presented nothing abnormal; motor power, freedom and precision of movement, and the muscular sense were unimpaired; knee-jerks decidedly increased; ankle clonus not present; the plantar reflex intact; electrical reactions normal. There was no rigidity, ataxia, or paralysis. Sensation to touch, temperature, and pain appeared to be unimpaired. The patient complains, however, of subjective sensations of numbness and pricking throughout the left lower extremity, including the foot, leg, and thigh. Similar sensations are referred to the foot and outer surface of the right leg, but they are not felt above the knee. Upon attempting to stand her legs bend under her, and unless supported she sinks to the ground. The irregular movements of the limbs are repeated much in the same manner at each effort to stand. They correspond closely to the description of Blocq * There are abrupt movements of flexion of the knees, followed by rapid extension; these contortions necessitate compensatory movements of the upper extremities and the head in order to maintain the equilibrium. Upon attempting to walk with some support these difficulties are increased; the

* Paul Blocq. Revue Generale de Clinique et de Thérapeutique, March 14, 1889, vol. iii., No. 11.

body is thrown forward, the thighs and knees are abruptly flexed, and then extended. These movements are wholly irregular. With some support she is able to move a short distance, but presently her legs bend under her and she sinks to the floor. She volunteers the statement that in order to obtain an article she desired she was able to cross the room upon her hands and knees.

The patient was kept in bed and not allowed to see members of her family or friends. Valerianate of zinc, in one-grain dose four times a day, was administered in gelatin-coated pills. She objected strongly to the oder of the pills, but nevertheless took them as prescribed. Once a day she had massage of the legs and feet for forty minutes; once a day faradism with the electrical brush for twenty minutes, the current falling just short of pain. At the end of two weeks she was allowed to get out of bed. The difficulty in standing and walking was much less. She was now given lessons in standing and walking. Her nurse was experienced and intelligent, and entered fully into the plan of the treatment. Improvement was rapid, and in ten days the patient was able to go about her room, and, assisting herself by the baluster, to go down stairs for a drive. In a few days the motor disturbance and the paræsthesia had wholly disappeared. About this time distinct hysterical phenomena—vomiting, intermittent tremor of the hands, vertigo, sensations of throbbing in the abdomen, emotional manifestations, weeping, and excitement without apparent cause—manifested themselves. There was no spinal tenderness; no tenderness over the so-called ovarian regions, and hysterogenetic areas were not found.

She was again isolated and placed under a systematic regimen. In the course of a month great improvement occurred, and it was thought well to send her to visit some friends at a distance who knew nothing of her sickness or its cause.

This case corresponds to the description of the condition by Blocq, who, in 1888, collated the instances, numbering at that time eleven, and gave to the affection the name astasia-abasia, now generally received. This observer defined the condition as a "Morbid state in which the impossibility of standing erect and walking normally is in contrast with the integrity of the sensibility, of the muscular strength, and of the co-ordination of the other movements of the lower extremities." (Knapp.)

With those who are familiar with Blocq's papers and that of Knapp it is quite unnecessary to discuss the theories of the causation of this condition. Church's statement that it is due to a systematized amnesia embodies that theory, which is generally accepted. That astasia-abasia is not a nosological entity but a syndrome must be conceded. In the foregoing case it was a symptom of hysteria. That it is usually such

a symptom, most of those who have seen cases believe. Osler speaks of it as "A manifestation of a neurosis allied to hysteria." Many of the cases have occurred in connection with organic disease. This fact does not militate against the hysterical origin of the condition, since cases of organic disease of the nervous system are often associated with hysteria.

In closing, I would call attention to the expressions used by my patient in describing her condition: "That her left leg felt as though it was made of cotton," and that she "felt like . . . a baby learning to walk." It is very remarkable that this girl, who has no knowledge of medicine or medical books, should have used the very phrases so often encountered in the writings upon the subject and at once descriptive of the condition and suggestive in view of the generally accepted theory of its causation.

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DISCUSSION.

DR. JACOBI: How many men are there among the recorded cases?

DR. WILSON: I do not know.

DR. JACOBI: I suppose there are but a small number, just as there are but a small number of hysteria cases observed among men.

DR. THOMSON: I have a record of a case of that kind which I have not published. It occurred in a Wall Street broker, who came to me on account of difficulty in standing, and because on many occasions he fell on the street. The only possible cause he could give me was that he had been passing through a great deal of business excitement.

CASES OF TYPHOID CHOLECYSTITIS ENDING IN RECOVERY.

By J. M. Da Costa, M.D., LL.D.,
of Philadelphia.

It is only of late years that we have recognized cholecystitis in typhoid fever, and it is generally looked upon as a very serious complication. So, indeed, it mostly is. In a paper which I presented last year to this Association, "On the Significance of Jaundice in Typhoid Fever," and which has been published in its Transactions, as well as in *The American Journal of the Medical Sciences*, July, 1898, I stated the results of fifty-eight cases of typhoid cholecystitis I had collected to be thirty-nine deaths and fifteen recoveries, while in four the result was uncertain or not mentioned. It would, therefore, appear that typhoid cholecystitis is fatal in over two-thirds of the cases; and in those that get well recovery in fully half the cases was the direct result of operative interference. Yet it is likely that, as we study the subject closely, and learn to recognize more readily this complication of typhoid fever, we shall find that the recoveries are more frequent than supposed. It is from the very grave cases, which alone have been mostly published, that our conclusions have been drawn.

To the list of recoveries from typhoid cholecystitis I can now add three cases, two of which happened in soldiers and one in a young girl. They were all under observation at the Pennsylvania Hospital.

Case I.—M. B., a soldier, aged thirty-two years, with typhoid fever, in which the Widal test on two occasions gave positive reactions, had many complications in the course of a long illness, such as phlegmasia dolens, otitis media, and swelling of the knees. There was a relapse on the twenty-ninth day of the disease, another one on the sixty-third day, and a third one on the ninety-third day; in the latter malarial organisms were found in the blood. It is not, however, the purpose to give a full history of this pro-

tracted and remarkable case, but rather to state that the deep typhoid infection manifested itself also in his gall-bladder, for in the second relapse tenderness was noticed in the upper part of the abdomen, chiefly below the ribs on the right side, and slight jaundice occurred; no tumor was to be felt. An examination of the urine showed bile-pigment, without albumin or sugar or casts being found; the urine was acid, its specific gravity 1020. The temperature, which in this relapse had reached 104° F., had declined to 98° when the jaundice was noticed. There were no marked gastric symptoms. The jaundice and the tenderness slowly passed away. Six days after bile was first detected in the urine this no longer contained it. The patient finally recovered, notwithstanding the many complications.

In this case, in which the profoundest typhoid fever infection was manifest, the cholecystitis was comparatively light. While there was pain in the region of the gall-bladder and sensitiveness, there was no tumor, and, except for jaundice, which, though slight, attracted attention, it is very likely that the disorder would have been overlooked. In the next case the symptoms were much more marked, and a tumor was evident.

CASE II.—C. E. B., a soldier, aged twenty-three years, had a severe case of typhoid fever, in which the temperature for thirteen days ranged between 104° and 105° F. There was diarrhœa and cough, and considerable pulmonary congestion, and, later, a bronchopneumonia on the right ride. On the sixteenth day of the disease, when the evening temperature was 104.6° F., soreness to the touch was noticed in the region of the gall-bladder; there was also pain in the abdomen, especially at the upper part, but at first no jaundice. Nor did the examinations of the urine show bile-pigment or sugar or casts. The urine had a specific gravity of 1009 and a trace of albumin. No vomiting occurred. Six days subsequently both pain and tenderness were found to be distinctly localized over the gall bladder, and a small, round tumor was palpable. No altered hue of the face or conjunctivæ was discernible, but the reaction for bile-pigment in the urine was very marked. The temperature ranged about 102° F., the stools were liquid, not offensive, nor materially changed; the tongue was clean; there was rigidity of the abdominal walls, especially on the right side. The patient expressed himself as greatly relieved by the local use of the tincture of iodine. Three days afterward the pain had gone, the temperature had declined, the swollen gall-bladder could be no longer felt. Recovery was complete, but not rapid.

This case is instructive, in showing how pain and tenderness, and even tumor, precede the icterus, which, indeed, may only manifest

itself by bile in the urine or be wholly absent. The temperature did not rise with the complication. It was high when this started, as it had been throughout the case, and declined, rather than advanced, with the decided manifestations of the malady. The symptoms were very clearly marked, but not violent, typically violent, as they were in the next case.

CASE III —Theresa L., aged eight years, was admitted on February 3, 1899, into the Pennsylvania Hospital, with typhoid fever. She had always been a healthy girl; with the exception of having had measles and whooping-cough some years ago, there was no history of disease. When admitted she had been ill for seven days with diarrhœa, cough, and fever. Her temperature was found to be 105° F., the pulse 142, the respirations 32. The liver dulness was small, the abdomen tympanitic; the urine had a specific gravity of 1020, and contained a small amount of albumin, but no casts. Some moist râles were detected at the lower part of the lungs posteriorly on the right side, but no dulness existed. The next day typical rose-spots appeared on the abdomen. The Widal test gave a positive reaction on the tenth day of the disease. The patient was treated by betanaphtol and very constant sponging, and though the case proved a severe one, the temperature for the first week of her stay in the hospital being often in the neighborhood of 104° F., and the urine having to be drawn by catheter, she did well, and by the twenty-seventh day of the disease it was noted that the temperature was normal or subnormal, with the exception on one occasion of a rise to 100° F.

Convalescence was looked upon as assured, when the child began to vomit, complained bitterly of pain in the abdomen, and the temperature went to 104° F. The pulse was 140. The question of perforation and peritonitis at once arose, as well as that of an appendicitis. But the high temperature and absence of collapse were against the former, and the fact that there was no tenderness or swelling in the right iliac fossa or at McBurney's point—indeed, that all the discomfort was at the upper part of the abdomen—set aside the latter. In the next few days the symptoms became more and more significant. The vomiting continued; at first curdled milk with bile-stained fluid, several ounces at a time, was rejected, then the same quantity of a pure, brownish, bilious fluid. Nothing was retained on the stomach—not even water—though a little later one-tenth of a grain doses of calomel stayed down, and small amounts of peptonized milk, and, still later, brandy and cracked ice; but the child had to be almost entirely nourished through the rectum, and sustained by hypodermatic injections of strychnine. There was some looseness of the bowels, and greenish stools were passed. The pain was very great, and she screamed with it; it was entirely referred to the upper part of the abdomen. Considerable tenderness over the region of the gall-bladder existed, and, on palpation, a tumor about the size of a lemon and having the shape of the gall-bladder could be felt and even seen through

the abdominal walls; both recti muscles were very rigid, the right especially; the tenderness extended to the left hypochondrium.

Applications of ice did some good, but the great restlessness of the child caused them to be exchanged for hot fomentations, which she liked better. The conjunctivæ at first were not discolored, but they became increasingly so, until the jaundice was very perceptible; the urine contained bile-pigment, but no albumin. The temperature—which, soon after the beginning of the attack, marked 101° F., with pulse of 124, and respirations 24—reached 104° F. for a short time, but it soon subsided, and the thermometer indicated between 99° and 101° F., while the tumor and pain were manifest. In the course of the case the whole abdomen became tumid, and the tenderness as marked in the left hypochondrium as in the right. The spleen did not appear to be enlarged; there was no ascites. Abdominal pain, tenderness, and tumor gradually subsided, though even toward the end of the case occasional pain in the region of the gall-bladder recurred. The child became greatly emaciated during the attack, and showed in her face the severe illness through which she was passing. But a gradual recovery took place, and she was discharged from the hospital on March 31st in good condition.

In reviewing this case, the violence of the pain stands out as the most prominent symptom. I have never in any instance of typhoid fever seen it equalled, and the child often shrieked with it. There was no doubt in her mind of its seat; when questioned she always put her hand to the region under the ribs on the right side. The pain was aggravated by the incessant vomiting. In the other cases reported in this paper the jaundice was slight; here it was very marked. The gravity of the symptoms made me think of asking one of my surgical colleagues to perform an operation; but as, when I was considering the propriety of surgical interference, improvement began to show itself, this was deferred, and the child recovered without. From the absence of sweating and chills—though this is not conclusive—I believed the cholecystitis not to be purulent, which influenced my decision. On the whole, this is the most marked case of typhoid cholecystitis ending in recovery that I have met with. It is worthy of note that it occurred after convalescence had set in. Cholecystitis in typhoid fever is a complication generally arising in the third or fourth week of the fever. In one of the cases reported in this paper it came on in the relapse.

The treatment in the cases detailed consisted for the most part in the administration of fractional doses of calomel, frequently repeated, in combating the nausea, and in the local use of ice or of poultices.

The former is to be tried first, and is, I believe, the more efficient. Counter-irritation with turpentine stupes or with iodine may also be used, and Case I. thought he derived much benefit from this. For the relief of the pain, hypodermatics of morphine may be necessary, and, as in Case III., the circulation may have to be supported by hypodermatics of strychnine and of digitalis.

FURTHER NOTES ON A CASE OF MALTA FEVER; A STUDY IN SERUM DIAGNOSIS.

By JOHN H. MUSSER, M.D., and JOSEPH SAILER, M.D.,
of PHILADELPHIA.

The following case has been previously reported in the *Philadelphia Medical Journal* for December 31, 1898. We desire to make a further report because, since that was published, several features of the case have developed which may, perhaps, be considered as invalidating our previous view of its nature. Moreover, it seems to us of considerable importance to determine positively whether Malta fever actually exists on this side of the Atlantic. Unfortunately, a positive bacteriological diagnosis could not be made. The micrococcus melitensis has rarely been obtained from the living subject, and then only by means of splenic puncture. In the present instance we did not consider that this procedure was justifiable. No attempt was made, moreover, to isolate the bacterium typhi abdominalis from the feces or urine. The procedure is of itself sufficiently difficult, and at no time were the clinical symptoms such as to justify, in view of the persistent absence of the Widal reaction and of the diazo reaction, the diagnosis of typhoid fever.

The case was reported December 31st. The last note was made December 21st. The patient was then suffering from fever of an undulating type that had been present upward of ninety days, and had been sixty days under our observation. During this time there was no evidence of any infection other than Malta fever, except a local and healing suppuration of the parotid gland, the pus from this yielding, on cultures made by Dr. Kneass, no pathogenic microorganism. It will also be remembered that typhoid fever, malaria, tuberculosis, and endocarditis had been excluded. We even thought an accidental syphilitic infection might have caused the fever. Indeed,

the only symptom was fever; the only suffering—and there was very little—was from the fever. The patient ate heartily, enjoyed the visits of his friends, and read the current news. Dr. Guitéras kindly saw him for us, and agreed he was suffering from some severe form of tropical fever, and agreed with us that the above-mentioned infections were not present.

Our record closed December 21st, when the patient, heartily sick of eighty days of hospital life, insisted upon leaving the hospital, and was sent home at his request, although his fever was then increasing, and on the day of his departure was 103°. After this the temperature continued to rise until it reached 105.2, and continued above 104° for eight days, when it fell to 101.2°, January 1, 1899. He returned to the hospital December 28th. In four days diarrhœa set in and continued for two weeks, or until January 9th. During this time the stools were often passed involuntarily. They were usually greenish-yellow. On January 3d the sheet was stained with an involuntary discharge of blood, scarcely one and a half ounces in our judgment—nevertheless, a hemorrhage—fresh, and seemingly from the colon. When the stools were not passed involuntarily their passage was attended by tenesmus and tormina. Had we not in mind the possibility of typhoid fever we would have said the intestinal condition was due to colitis. The thought that this was possible was intensified by the fact that the liver was enlarged and painful. It extended from its highest normal limits to two inches below the margin of the ribs.

Subsequently, the temperature was of the remittent type, with marked variation. It fell to 101° January 1st. It then assumed an undulating type, the great diurnal variation continuing until the one hundred and thirty-third day of the disease. On this day there was a difference of 2.8° between the morning and afternoon temperatures, although the evening rise was only 98.8°, the morning temperature being 96°.

During the period of diarrhœa the abdomen was tympanitic and an eruption of an erythematous and papular character developed over the trunk. The spots were larger than typhoid spots and darker red in color. They did not appear in groups.

During this time he lost memory for recent events and a curious confusional delirium was present for about one week.

SERUM DIAGNOSIS. The onset of symptoms resembling those of typhoid fever in this most interesting case, which thus far had showed no signs of this infection, led us to renewed efforts to study the serum reactions. One of us, conjointly with Dr. Kneass, made frequent tests all of which were negative. As further control we asked Dr. Stewart, of the City Laboratory, to determine the reaction also. These tests were made every second day long into convalescene. At no time did Dr. Stewart secure the Widal reaction to indicate the presence of typhoid fever. The diazo reaction was studied by Dr. Wadsworth and was invariably absent.

The first culture of the micrococcus melitensis was obtained from Dr. Kinyoun about December 21st. The blood of the patient was diluted in the white pipette in the proportion of 1 to 22. A reaction made with this showed typical agglutination in small clumps at the end of twenty-six minutes. Unfortunately, the tube was broken while making reinoculations. A second tube was obtained about two weeks later. It also gave a typical reaction both by the wet and the dry method on various occasions, the last being April 25th. On almost all occasions the blood was also tested with cultures of typhoid bacilli, and failed in every instance to present any trace of agglutination.

A culture obtained through Dr. Kelly from Dr. Kretz, of Vienna, showed two types of growth. The first appeared on agar on the second day after inoculation. The colonies grew luxuriantly all along the course of the stroke and rapidly acquired a bright-yellow color, resembling a culture of staphylococcus citreus. It failed to react with the blood of the patient. The other micro-organisms did not appear on the culture medium until the seventh day after inoculation. It grew at first along the streak as grayish-white translucent colonies, then in time these became confluent and formed a white semi-translucent growth. With this culture Dr. Kelly obtained a doubtful reaction in about an hour by the dry method. The culture obtained from Dr. Kinyoun was studied by Dr. Kneass, who states that it appears the third day after inoculation upon agar as a thin, pale, grayish growth. With this culture all the reactions were performed, the maximum period, before agglutination took place, being twenty-six minutes on the first occasion, and the minimum period being four minutes.

The micro-organism is about 0.5 μ in diameter, is non-motile, but shows Brownian movements. It conforms in its biological properties

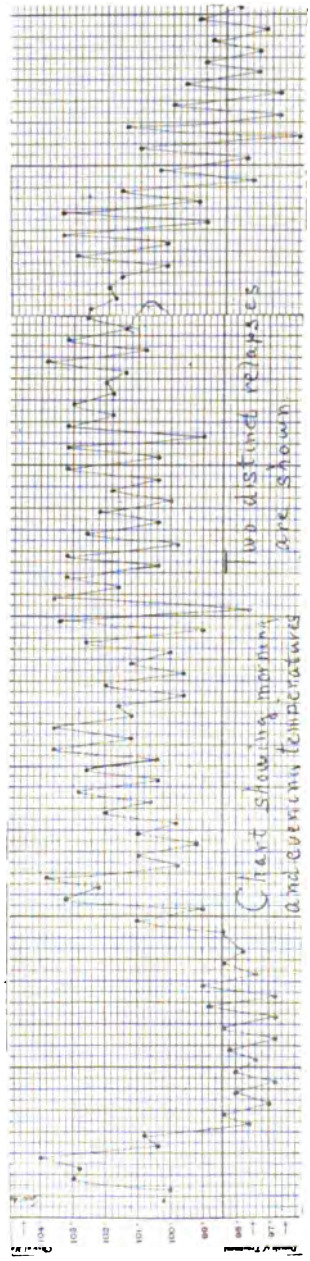
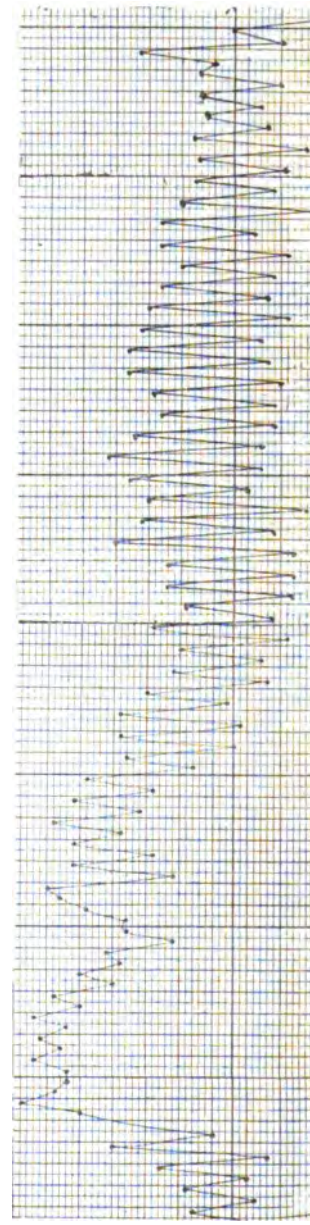


Chart showing morning and evening temperatures
Two distinct remissions are shown
104
103
102
101
100
99
98
97



with the micro-organism described by Bruce,[1] except the rapidity with which the colonies appeared after reinoculation. Agglutination appears to occur when, as a result of the oscillations, the micro-organisms come in contact, when they adhere and cease moving. The clumps are, therefore, much smaller than those observed in the case of the Widal reaction in typhoid fever.

We have then a case of what appeared to be Malta fever, presenting in the termination of its course phenomena allied to those of the typhoid infection, but without the serum reaction of this infection. The natural question that arises is, Was the disease typhoid fever from the first? We believe it was not. The clinical history is against it; the serum diagnosis does not prove it. Agglutination was never secured with typhoid bacilli, and was repeatedly secured with the cultures of the micrococcus melitensis, with all control precautions.

We are personally of the belief that the serum diagnosis is final in infectious disease unless there is a pronounced mixed infection, and although this is not impossible in the case we have reported, the absence of the Widal reaction and the atypical course of the symptoms excludes, we believe, the probability of typhoid infection during the latter part of the disease. Aside from the absence of involvement of the joints, the clinical history resembles closely the description as given by Bruce, and the presence of the serum reaction confirms, we believe, the diagnosis.

[1] Twentieth Century Practice of Medicine, vol. xiv. (This article contains a full bibliography.)

SMALL ANEURISM OF THE DESCENDING ARCH OF THE AORTA; X-RAY EXAMINATION CONFIRMED BY AUTOPSY.

By FRANCIS H. WILLIAMS, M.D.,
OF BOSTON.

In the *Medical and Surgical Reports of the Boston City Hospital* for 1897 I reported some cases of thoracic aneurism that I had seen in 1896 by means of X-ray examinations. Since then I have seen a number of others, as well as cases in which there were symptoms pointing to aneurism of the thoracic aorta, but in which the X-ray examinations show that no aneurism was present.

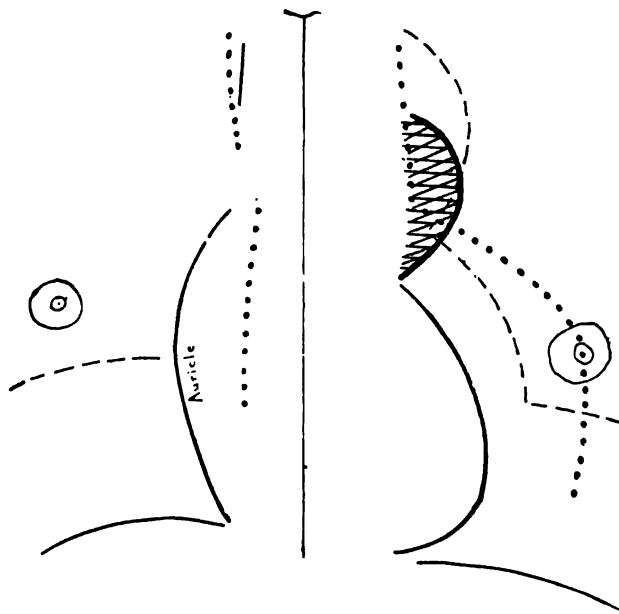
The following case is noteworthy because the aneurism was small, and an opportunity was given, by the death of the patient from another cause, to see that the X-ray and post-mortem appearances agreed exactly. The patient was referred to me for an X-ray examination by Dr. H. D. Arnold, February 18, 1899. It was thought probable that he had an aneurism of the innominate artery, and there was a question of aortic aneurism as well. Dr. Arnold's examination is in part as follows:

T. H. Y., forty-five years old. Pain in the præcordia for about one week, increased on exertion; sense of intense pressure there. Some cough and expectoration; slight attack of hoarseness in past few days. Physical examination: Area of dulness shown in diagram by dotted lines. At lower angle of the neck on the right side, close above the inner end of the clavicle, pulsation is more marked than normal, and greater than at corresponding place on the left side of the neck. Pulsation is greater than normal in the episternal notch. Pulsation in the episternal notch is felt more distinctly on the right side than on the left, and there is a distinct lateral thrust from the right, instead of from below upward; there is a slight tracheal tug.

February 18. X-ray examination showed a small aneurism of the descending arch of the aorta. The examination was made with the patient lying on his back (Fig. 1), and later when lying on his face.

On February 23d the patient was found on the street and brought to the hospital in an unconscious condition, and placed in my service. He died just after entrance.

FIG. 1.



Tracing of outline seen in the fluoroscope and drawn on the chest, and of the lines obtained by percussion.

Full lines, except the median line, represent X-ray outlines in full inspiration, broken lines in expiration; the shaded area shows the position of the aneurism in full inspiration, the broken lines above it its position in expiration; dotted lines, the outlines as seen by percussion. Another tracing of the aneurism, made on the back, showed a movement downward of only 1¾ centimetres, while this tracing made on the front of the chest had about double this movement. Both are more than the real up-and-down movement of the aneurism between expiration and full inspiration, as the aneurism, though nearer the fluorescent screen when the screen is on the back than when on the front of the chest, is in either case far enough away from it to cause the shadow of the aneurism to move further than the aneurism itself.

A careful post-mortem examination by Dr. Pearce showd an aneurismal dilatation of the innominate artery, and an aneurism of the descending arch of the aorta, which corresponded to the outline which had been traced at the X-ray examination, and had been brought to the autopsy-room for comparison. The outline of the right auricle and of the left ventricle (Fig. 1), made by means of the X-rays, also corresponded to what was found at the autopsy.

It will be seen by comparing the tracing from the X-ray lines drawn on the front of the chest, with the dotted lines, which repre-

sent the outlines by percussion, that we failed to recognize any dulness over the site of the aneurism, and even after I had *seen* its outline on the fluorescent screen we could not detect it by percussion. Further, by following the dotted line, which indicates the left border of the heart found by percussion, we see that it is incorrect when compared with the same border as determined by the fluorescent screen and at the autopsy. On the right side the border of the enlarged right auricle was not recognized by percussion, but I saw it on the fluorescent screen, and, as already stated, this X-ray outline was confirmed at the autopsy. In cardiac disease I have frequently demonstrated a marked discrepancy between the position of the borders of the heart as suggested by percussion and as determined by means of the fluorescent screen.

In certain aneurisms of the aorta (larger than the one here described, but not of excessive size) I have observed that the excursion of the diaphragm on the left side was only one-third or less that of the right side; this shortened excursion is probably due to the pressure of the aneurism on the left bronchus.

A further point of interest in this patient is that the lungs were found to be normal both by the X-ray and post-mortem examinations.

Fig. 2 shows my method of examining the thorax. One end of the static machine is seen in the right of the picture, where the curtain, which hides the machine during an examination, has been drawn aside. An aluminum screen, which is grounded (not shown in the picture), is placed between the Crookes tube and the patient as a protection to him. I have never seen any burn or untoward result occur in about 3000 X-ray examinations which I have made.

The patient may be examined sitting up or lying on a stretcher, as seen in Fig. 2; if too ill to walk from the ward he is brought to the X-ray room on the stretcher, which fits into notches on the wooden horses seen in the photograph.

In examining the thorax the anode of the Crookes tube should usually be placed under the point where the median line is crossed by a line joining the nipples—that is to say, on the level with the fourth ribs, between three or four feet away from the fluorescent screen. The median line is obtained by sighting from the plumb line seen at the feet of the patient to that at the head; the other point is got by hanging a line seven feet in length and weighted at

FIG. 2.

Curtain drawn aside at foot of stretcher to show position of static machine.

either end (not shown in the cut) across the patient over the fourth ribs, and sighting, as before, from weight to weight.

The fluorescent screen lies on the patient's chest, and over the screen has been placed a transparent sheet of celluloid, on which the desired outlines of the heart and diaphragm, for example, may be drawn. These outlines may be readily traced on ordinary paper from the celluloid, and, when properly labelled, kept as a note of the case. The lines on the celluloid may then be rubbed out and the celluloid used again.

ON THE INTERPRETATION OF PULSE-TRACINGS.

By ARTHUR R. CUSHNY, M.D.,
OF ANN ARBOR.

ALTHOUGH the physiology of the mammalian heart is much more accurately known than that of most other organs, and though the study of the pulse has engaged the attention of clinicians from the earliest dawn of medical science, it is remarkable how little has been done to bring the experimental and the practical aspects of the subject into connection. It is true that the explanation of the undulations on the pulse-tracing and of the modifications of these observed in disease has been the subject of a large number of investigations, but no attempt has been made to solve the question of the causes of the irregularity of the pulse. Of late years several writers have insisted upon the importance of the auricle as a factor in the irregularity, but, with the exception of Radasewsky's paper, I have been unable to find any account of pathological examinations of the auricle in cases of irregular pulse.

My attention was drawn to the subject by the results of a series of experiments performed some years ago with Matthews, and during the last year I have had, through the kindness of Dr. Dock and his staff, an opportunity to examine a considerable number of sphygmographic tracings taken in cases of irregularity of the pulse. I propose in the following pages to give the results of an attempt to interpret these clinical observations in terms of laboratory experiments.

The object of our experiments, which were performed on dogs, was to ascertain the effects of a single stimulus applied to the heart. It is unnecessary to revert to most of our conclusions, which bear upon physiological rather than on practical points, and which have been recorded elsewhere.[1] Let it suffice to state that the movements of the auricle and ventricle were recorded separately by a system of levers, and that in a number of instances a sphygmographic tracing

[1] Journal of Physiology, xxi. p. 213.

was taken simultaneously from the carotid artery. When a single electric shock was passed through the ventricle at any time, except in the refractory period, it was followed by a premature contraction of that chamber (Fig. 1). In many instances this contraction expelled

FIG. 1.

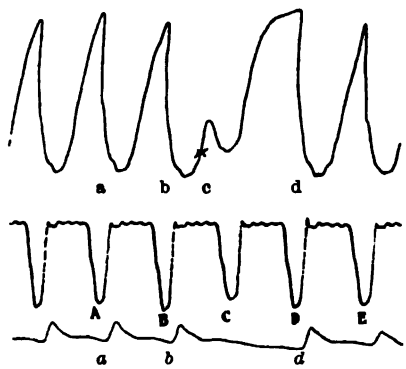
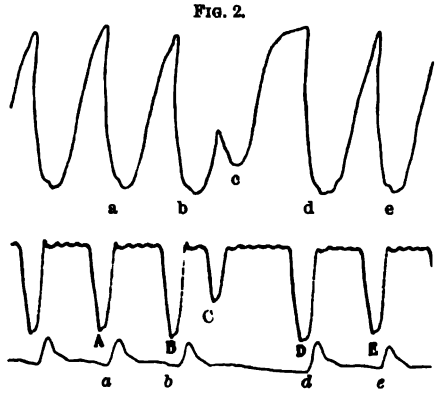


FIG. 2.



Myocardiograms and sphygmograms from the dog. (See text.)

sufficient blood to cause an undulation in the sphygmographic tracing, this undulation being lower than that caused by a normal pulse, and occurring at a shorter interval than usual after the last ordinary elevation. But, as a general rule, the contraction of the ventricle was too feeble to cause a pulse-beat. In Fig. 1[1] a premature systole of

[1] In Figs. 1 and 2 the uppermost tracing was drawn by the ventricle, the next by the auricle, the third by a sphygmograph (Frey's) attached to the carotid artery. During systole the auricular and ventricular levers made a stroke downward. During diastole they rose again.

the ventricle was induced by an electric shock which reached that chamber at the point indicated by the cross-lines in the ventricular tracing. It was followed by a premature systole (c), which was in turn succeeded by a relaxation, and the ventricle then remained quiescent until it was roused to activity (d) by an impulse descending from the auricle. The auricular rhythm was unaffected by the irregularity of the ventricle. If the course of each impulse be followed from the auricle to the ventricle and finally to the pulse, it is found that A is followed by a and then by *a*, B by b and then by *b*. But C beginning in the auricle has no effect on the ventricle, because it reaches it during the premature systole, c. D, however, is followed by d and later by *d*, and the normal sequence is reinstated. The interval between the normal pulsations of the artery, *b* and *d*, or between the ventricular systoles, b and d, is determined by that between the auricular contractions, B and D. And as the auricular rhythm is perfectly regular throughout, the distance B–D is twice that of B–C, or twice A–B, or D–E, etc.—that is, the interval between the two normal pulsations of the artery, or the length of the intermission, is equal to twice the usual interval between the two pulsations.

A little consideration will show that as long as the auricle is beating regularly an intermission which is induced by a failure of the ventricle to contract must always be equal to twice the ordinary interval of the pulse. For example, if there had been no premature ventricular contraction (c) in Fig. 1—*i. e.*, had the ventricle relaxed and remained quiescent until it was aroused by the impulse D—the length of the intermission would be the same. So that a general law may be formulated, that an intermission which is due to ventricular disorder, and during which the auricle continues to contract regularly, must always be equal in length to twice the ordinary pulse-interval.

When an electrical shock is passed through the auricle (Fig. 2), a premature systole is caused in this chamber as in the ventricle in Fig. 1; it does not remain limited to the auricle, however, but is transmitted to the ventricle, which contracts prematurely, as if it had received a direct stimulus; a weak premature pulse is sometimes seen in the artery, but here, too, the blood expelled is generally too small in amount to cause any appreciable movement, and the tracing displays again a complete intermission. In Fig. 2, A gives rise to a and indirectly to *a*, B to b and *b*, and C to c, which is not followed by a

distinct movement in the artery. The next normal auricular systole, D, is followed by d and *d*, and E by e and *e*. The only difference between Figs. 1 and 2 appears at first sight to be the irregularity of the auricle, and, as this is not visible in the sphygmographic tracing, it might be supposed that an irregularity of auricular origin is followed by the same changes in the pulse as one arising from ventricular disorder. When the sphygmographic tracing is subjected to accurate measurement, however, a difference is observed in it; the intermission is shorter than twice the ordinary pulse-interval. For example, if the intervals between *a* and *b*, *b* and *d* and *d* and *e* be measured, it will be found that *a*–*b* and *d*–*e* are each equal to $\frac{27}{50}$ second. If the intermission b–d were twice the normal interval, it would last $\frac{54}{50}$ second, but in reality it is only $\frac{49}{50}$ second in duration. The explanation of this point is simple—the auricle gives rise to the rhythm of the heart; the impulse leading to the contraction, D, is not derived from any higher rhythmical organ, but arises from the auricle itself. When the auricle has collected enough energy or irritability to cause a contraction, the systole follows, this chamber not waiting for some impulse from without as the ventricle does.

The exact length of the intermission in these stimulation experiments varies with the point in the auricular cycle at which the electric shock is given, but it is unnecessary to enter upon this here. The important fact is that in these experiments the intermission is always shorter than twice the ordinary pulse-interval. Consideration will show that here again a general rule may be formulated, that the intermissions due to auricular disorder (disorder of the part of the heart which emits the rhythmical impulses) are not necessarily equal in length to twice the ordinary pulse-interval, for the auricle may stand still for any interval of time and then resume its contractions. It is not necessary that it should contract at the exact time at which it would have done so normally, any more than it is necessary that if the breath be held for some time the first inspiration will follow at any definite moment. When the probabilities of the case are considered, it will be seen that the chances of the auricle recommencing its contractions at the end of a double pulse-interval are small. The irritability of this chamber increases very rapidly when it is quiescent, and in most cases must reach the exploding point sooner than two full intervals.

These experiments may be considered a sufficient basis for the general statement that intermissions of the pulse which are due to ventricular disorder must be equal in length to two normal intervals, while those that are of auricular origin may be of this length, but in the great majority of cases are shorter. Conversely, the intermissions of the pulse which are equal to two ordinary intervals are in all probability ventricular in origin; those which are shorter are certainly not ventricular, and are therefore due to auricular derangement.

A few examples of the duration of the intermission in the dog's pulse under stimulation of the ventricle and auricle may serve to elucidate this question (Table I). It may be stated that these do not by any means exhaust the numbers at my disposal, for I have made a long series of experiments on the subject, and have measured some hundreds of intermissions, all of which gave the same result without exception. I have selected some of the measurements of only two of these experiments, however, which are sufficient to give an idea of the extent of the variation in the length of the intermissions. Where the stimulus resulted in a premature arterial pulse, the intervals before and after it are enclosed in brackets, in order to allow a comparison with those in which there was a complete intermission.

TABLE I.

	A. Normal pulse-interval.	B. Chamber stimulated.	C. Inter-mission.	D. (2 A—C).	E. $\left(\frac{D}{A}\right)$	Average of E.
Expt. A.	54	Ventricle.	107	1	1/54	
	55	"	110	0	0	0
	54	"	108	0	0	
	54	Auricle.	98	10	10/54	
	53	"	92	14	14/53	
	52	"	100	4	4/52	
	54	"	100	8	8/54	
	53	"	98	8	8/53	2/9
	55	"	88	22	22/55	
	55	"	93	17	17/55	
	54	"	98	10	10/54	
	54	"	91	17	17/54	
Expt. B.	40	Ventricle.	79	1	1/40	
	39	"	78	0	0	0
	40	"	80	0	0	
	39	Auricle.	62	16	16/39	
	38	"	64	12	12/38	
	39	"	(27+42) 69	9	9/39	
	38	"	62	14	14/38	1/3
	38	"	65	11	11/38	
	38	"	67	9	9/38	
	38	"	62	14	14/38	

In column A, the duration of the normal interval is given in hundredths of a second; in column B, the part of the heart stimulated; in column C, the length of the intermission in hundredths of a second; in D, the extent by which this fell short of two intervals (2 A–C), and in E, the fraction of a pulse represented by this deficiency $\left(\frac{D.}{A}\right)$

In this table it will be observed that when the ventricle is stimulated, the intermission is equal to a double interval, the greatest deviation from this amounting to only $\frac{1}{64}$ and $\frac{1}{40}$ of the normal pulse-interval, numbers which may well be considered within the limits of error. When the stimulus is applied to the auricle, on the other hand, the resultant intermission is invariably shorter than a double pause, the deficiency varying from $\frac{1}{13}$ to about $\frac{2}{5}$ of a normal pulse-interval, according to the exact point in the cardiac cycle at which the stimulus is received. It may be remarked that the deficiency seems to differ in different hearts, that in Experiment B being distinctly greater than that in Experiment A. In the second experiment the auricle seems to regain its irritability sooner than in the first, and this is perhaps connected with the fact that the rhythm is faster in the second.

When one attempts to apply the principles deduced from animal experiments to the analysis of clinical sphygmographic tracings, one is met by the difficulty that in some of these the pulse is so irregular that no normal interval can be ascertained with certainty. I shall pass over these at present, and shall deal at first with tracings in which the rhythm is regular on the whole, but in which intermissions occur at regular or irregular intervals. In these, also, there are small differences in the pulse interval, and even in perfectly normal individuals a considerable variation has been shown to exist by Von der Mühll.[1] These variations seldom amount to more than one or two hundredths of a second, however, so that they do not materially affect the results. In order to eliminate the error, as far as possible, I have generally taken the average of the three or four pulses preceding and following the intermission, and thus obtained an average interval, which was compared with that immediately preceding and that immediately following the intermission. In this way certainty could be reached

[1] Deut. Arch. f. klin. Med., xlix. p. 348.

that the interval taken as a basis for the calculation really was that which would have occurred had no irregularity been present. The tracings were taken with Jacquet's sphygmochronograph, which is the only instrument available when such minute intervals as $\frac{1}{100}$ second have to be dealt with. In analyzing the tracings I have used his curve-reader (curvenanalysator), which was kindly put at my disposal by Prof. Lombard. A number of tracings were taken in each case, and the intermissions were all carefully measured and an average taken of their duration, or rather of the extent to which they fell short of a double interval. Only in this way can any reliable results be attained, as not infrequently one individual intermission may appear to be of auricular origin, while, when it is compared with the series, it is seen to be really ventricular.

In Table II., I have arranged a series of intermissions which approach the type which was found to be caused by ventricular stimulation in the dog. The columns correspond to those of Table I., the second being omitted.

TABLE II.

Case.	A.	C.	D.	E.	
L.	57½	116	+1	+1/57½	Admitted for cataract. Pulse often perfectly regular; at other times every fourth beat is missed (Fig. 5).
	58	114	2	2/58½	
	59	117	1	1/59	
	56½	112	1	1/56½	
	55½	116	+5	5/55½	
	55	105	5	5/55	
	56	113	1	1/56	
	57½	115	0	0	
	Average approximately ½			1/100	
M.	55	111	+1	+1/55	Pernicious anæmia, mitral regurgitation, dilatation of the heart with systolic murmur; pulse small, quick, irregular in volume and rhythm, with occasional intermissions. Post-mortem: Small hemorrhages under pericardium; right auricle much dilated, other chambers normal size; mitral orifice small, and posterior flap shortened (Fig. 3).
	51½	99	4	4/51½	
	54	107	1	1/54	
	54	112	+4	+4/54	
	55	109	1	1/55	
	53½	111	+4	+4/53½	
	56	110	2	2/56	
	Aver. approximately		+1/7	+1/54 × 7	
H.	62½	126	+1	+1 62½	Recurrent appendicitis; pulse regular except for occasional intermissions (Fig. 4).
	59½	122	+3	+3 59½	
	61	120	2	2 61	
	60½	121	0	0	
	Average		½	1.120	
Mc.	47	95	+1	+1/47	Cancer of the breast, age 56. Pulse fairly regular, but occasionally misses a beat.
	46	91	1	1 46	
	44½	89	0	0	
	Average approximately		0	0	

Case.	A.	C.	D.	E.	
W.	64½	128	1	1/64	Hernia, age 22. Pulse ordinarily regular, but often misses every third beat for several minutes at a time.
	65	126	4	4/65	
	64½	124	5	5/64½	
	65	126	4	4/65	
	60	120	0	0	
	Average		3	1/20	
Mg.	77	154	0	0	Retention of urine, age 59. The pulse occasionally misses a beat, but is generally regular.
	76½	152	1	1/76½	
	80	157	3	3/80	
	Approximate average		1	1/60	
B.	59 (46+73)	118	+1	1/59	Student, complains of irregularity of heart, lasting for several minutes at a time, and then passing off (Fig. 12).
	58 (45+70)	115	1	1/58	
	60 (46+74)	120	0	0	
	Average		0	0	

In Table III. are arranged the intermissions which approximated those observed in the dog on stimulation of the auricle.

TABLE III.

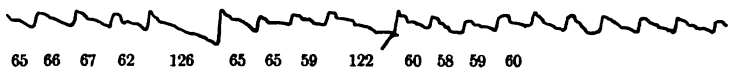
Case	A.	C.	D.	E.	
N.	68	119 (46+73)	17	1/4	Atheroma, age 78. Pulse often regular for days at a time, and then occasional intermissions for several hours.
	73	123	23	23/73	
	Average		19	1/4	
Q.	93	163	23	1/4	(Fig. 6).
	97	170	24	1/4	
	Average		24	1/4	
G.	77	123	31	2/5	
	74	129	19	1/4	
	70	124 (46+78)	16	1/4	
	71	118	24	1/3	
	Average		22½	1/3	
St. C.	110	179	41	4/11	Atheroma, age 66. Heart-sounds weak, no murmur; radial arteries tortuous and hard; pulse 60, irregular in rhythm and volume, occasionally missing a beat (Fig. 7).
	100	167	33	1/3	
	Average		37	1/3	
Sh.	65	122	8	1/8	Blacksmith. Dilatation, hypertrophy, double aortic lesion, mitral regurgitation, no tricuspid regurgitation: general anasarca; pulse often misses a beat. Post-mortem: Great distention of all the chambers, distinct separation of the muscular fibres in the auricles (Fig. 11).
	72	134	10	1/7	
	69	115	23	23/69	
	71	127	15	15/71	
	66	114	18	18/66	
	Average		15	2/9	
K.	69	118	20	2/7	Surgical case, age 77. Pulse often misses a beat, and in the intermission a premature pulsation is often present. Sometimes several intermissions occur in succession (Figs. 9, 10).
	58	100	16	1/4	
	57	100	14	1/4	
	65	110	20	1/3	
	63	104	22	1/3	
	62	105	19	1/3	
	64	110 (40+70)	18	1/4	
	69	114	24	1/3	
	Average		17	5/16	

FIG. 3.

59 59 56 59 116 58 58 59 56 56

Fairly regular sphygmogram, with occasional intermissions due to ventricular extra-systoles.

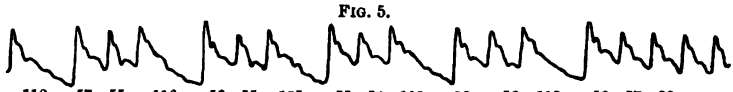
FIG. 4.



65 66 67 62 126 65 65 59 122 60 58 59 60

Fairly regular pulse, with frequent intermissions. The second of those in the tracing appears to be due to ventricular extra-systole, as there is a distinct elevation in the descending limb of the curve, so that all the intermissions are probably really of this origin.

FIG. 5.



112 57 55 116 56 55 105 55 54 113 58 56 115 59 57 58

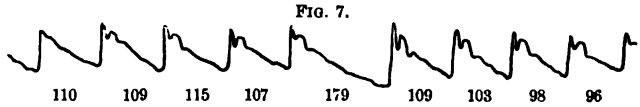
Pulse with every fourth beat intermitted, owing to ventricular failure or extra-systole. The pulse was often perfectly regular for hours at a time.

FIG. 6.

97 97 93 88 163 84 78 76 78

Pulse with intermission shorter than two-pulse intervals, and, therefore, of auricular origin.

FIG. 7.



110 109 115 107 179 109 103 98 96

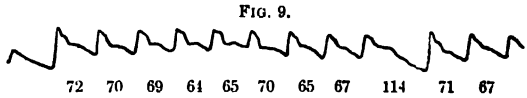
Pulse with auricular intermissions at irregular intervals

FIG. 8.

79 79 80 77 147 83 79 145 84 118 83 81 147

Pulse with every fourth beat intermitted, owing to auricular disorder. (Contrast Fig. 5.)

FIG. 9.



72 70 69 64 65 70 65 67 114 71 67

Pulse of somewhat irregular rhythm presenting one intermission of auricular origin.

In Table II. the average deviation from a double pulse-interval varies from zero up to $\frac{1}{20}$ of a pulse-interval. In regard to the fifth case (W.), I had some doubt as to whether it should be placed in Table II. or Table III., and the number of tracings at my disposal were scarcely sufficient to allow of a certain interpretation. In Table III. the average intermission was $\frac{1}{4}$–$\frac{1}{3}$ of a pulse-interval shorter than two pulse-intervals.

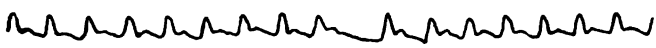
When the second and third tables are compared with the first there is noted a very striking resemblance between the intermissions due to ventricular disorder and Table II., and those due to auricular stimulation and Table III., and this may be regarded as sufficient grounds for the theory that the disorder in the hearts from which Table II. was derived was ventricular, while those corresponding to the tracings

FIG. 10.

68 118 119 116 70 65 66 65 111 115 115 114 112

Pulse showing frequent intermissions of auricular origin. Every second beat omitted toward the end, owing to auricular extra-systoles.

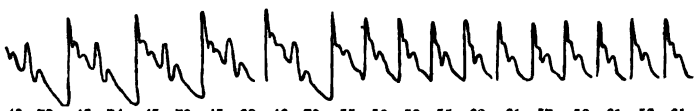
FIG. 11.



70 68 66 65 68 64 122 75 67 66 65 64 65 67

Irregular pulse, with occasional intermissions from auricular disorder.

FIG. 12.



46 79 46 74 45 70 45 68 46 73 55 59 59 55 62 61 57 59 61 56 61

Pulse regular toward the end of the tracing, but presenting irregularities in the beginning. The large contractions are induced by the auricular impulse, the smaller ones arise from ventricular extra-systoles.

analyzed in Table III. labored under disease of the auricle. I may state here that these are not selected tracings, but are derived from thirteen out of the first fifteen cases of irregularity of the heart which I had an opportunity of examining in the last year. The two remaining cases I have not included in the tables, because the rhythm was so irregular that I found it difficult to estimate the exact pulse-interval.

In thirteen out of fifteen cases, then, the diagnosis between auricular and ventricular disorder could be made with a great degree of certainty. In the other two cases the irregularity was almost certainly auricular, for no intermission was as long as two other pauses. The only other explanation of the irregularity would be that the ventricle had taken a complete idioventricular rhythm, and did not wait for the auricular impulse for any one systole. In this case the rhythm might be irregular from ventricular disorder, and yet the intermissions would not amount to a double pause in length, as we showed in a previous paper. But this contingency is so unlikely to occur in man that it can be neglected with perfect safety, and I have no hesitation in classifying the irregularities in all of these cases, except the seven of Table II., as due to auricular disorder.

The further question arises as to what is the cause of the intermission of the ventricle or auricle in these cases. The heart may fail to cause a pulse-wave, firstly, because the ventricle contains so little blood when it executes a premature contraction that the arterial pressure is not increased enough to move the lever on the artery, or, secondly, because the ventricle does not contract at all. A very important contribution to this subject has been made by Wenckebach[1] since I commenced my studies, and I must congratulate this observer on being the first to break ground in what may prove to be of great scientific and practical interest. He discusses almost exclusively the intermissions which are equal to two pulse-intervals, and comes to the conclusion that these are invariably due to premature idioventricular contractions. The grounds on which he founds this statement are twofold: in the first place he was able in every case to make out by auscultation a double contraction-sound in the beginning of the intermission, and in the second place a pulse-tracing, which at one time shows a complete intermission, very often shows soon afterward, an intermission interrupted by a weak premature elevation. He seems to have observed this in the great majority of his cases, and I have met the same indication very frequently in my own less extensive investigations. These intermissions, therefore, are identical in every feature with those obtained in my experiments on the dog, except that in man the ventricular stimulus is idioventricular, while in my

[1] Zeitschr. f. klin. Med., xxxvi. p. 181.

experiments it was external. In a number of instances, however, I have observed a premature systole in the dog without any electrical stimulus having been supplied, and in these cases the intermission was identical in every feature with that observed in the human pulse. In a very considerable number of instances, therefore, the pulse intermission is due to a premature systole of the ventricle.

It may be questioned, however, whether this is true in every case, for in one of our patients the most careful stethoscopic examination failed to detect any contraction sound during the intermission, and I am inclined to regard the irregularity in this case as due to the complete failure of the ventricle to contract. The impulse from the auricle either failed to reach the ventricle or was unable to excite a contraction in it. Unfortunately, I neglected to examine the other cases in regard to this point, but this experience seems to indicate that Wenckebach's explanation is too sweeping. If the ventricle fails to contract for any reason, the intermission is, of course, of the same length as if it were due to a weak premature contraction. This failure to contract may be due either to disorder of the communicating fibres between the auricle and ventricle or to disease of the ventricle itself. It is quite impossible to determine at present which of these is the determining cause of ventricular intermission, and, as in the majority of instances these intermissions appear to be due to a premature contraction, it seems unnecessary to pursue this subject further at present.

As regards the intermissions which are caused by auricular derangement, the cause is unquestionably a premature contraction in a certain number of instances. This is demonstrated by the appearance of a distinct undulation in the pulse-curve in certain cases, while in other tracings a number of complete intermissions may be interrupted by one which shows a distinct premature pulsation.

Very little is to be learned from the literature of the heart in regard to lesions of the auricle. The only observations which I have been able to find are those of Radasewsky,[1] who made a detailed examination of the histology of the heart in six cases, and found that in one in which there had been no marked irregularity before death the ventricle alone was diseased; in four in which the auricle presented

[1] Zeitschr. f. klin. Med., xxvii. p. 387.

more marked lesions than the ventricle there had been marked irregularity and intermission of the pulse, while in one in which the disease of the auricle and ventricle was less extensive the rhythm had been regular.

In one case in which the pulse demonstrated clearly that the intermissions were auricular in origin (Table III., Sh.), the autopsy showed an enormous dilatation of all the chambers, and the muscular fibres of the auricle could be seen to be separated from each other by distinct clefts. No histological examination of this heart has been made as yet.

Every case in which the pulse shows distinct auricular intermissions is not to be regarded as one of serious disease of this chamber, for a very considerable proportion of perfectly healthy persons show this occasional lapse. For example, one of my tracings (Fig. 13) shows

FIG. 13.

Irregular pulse from excessive inhibitory activity. The intermission might be mistaken for an auricular failure.

an irregular rhythm which ordinarily varies from fifty-four to sixty one-hundredths of a second pulse-interval, but at intervals shows intermissions of ninety to one hundred. This tracing puzzled me for some time, until I noticed that the intermission always occurred at a definite point of the respiration, and could be induced at any time by taking a deep breath, when I realized that it was due to excessive activity of the inhibitory centre. As is well known, this centre is peculiarly sensitive in certain individuals, and in this case it is capable of arresting the heart for some time, and thus giving rise to an intermission. The whole heart is arrested and the intermission is, therefore, of the auricular type. Exactly the same phenomenon can be elicited in animals by stimulating the pneumogastric nerve in the neck for a fraction of a second. This inhibitory intermission is liable to be confused with the true auricular intermission, but is generally followed by a second prolonged interval, which may serve to indicate its true nature. In case of doubt, it could be diagnosed by its disappearance when the inhibitory mechanism is paralyzed by

atropine. Dehio[1] has observed arhythmia of the pulse disappear under this treatment in a number of cases.

The occurrence of this false auricular intermission suggested the question whether in some cases ventricular intermissions might not be due to inhibition, for it is well known to physiologists that stimulation of the pneumogastric nerve retards the passage of impulses from the auricle to the ventricle, and also renders the latter chamber less susceptible to impulses. It is therefore conceivable that some of the ventricular intermissions might be inhibitory in nature, that the impulse descending from the auricle fails to reach the ventricle, or finds it so depressed that it does not respond. Further consideration dispels this doubt, however, for the inhibitory action has to be so powerful before the ventricle or the communicating fibres are acted on that the pulse would present an extraordinarily slow rhythm, about twenty to thirty per minute or less.

In conclusion, I have to acknowledge my indebtedness to my colleague, Dr. Dock, for his kindness in putting his tracings at my disposal, and to Drs. Arneill and Boyce for the help they have afforded me in various ways, particularly in collecting tracings which bore on the subject of investigation.

DISCUSSION.

Dr. Dock: I brought with me the heart of the patient Dr. Cushny has just spoken of and will pass it around. The patient was admitted with marked loss of compensation; there was a double murmur in the aortic region, at times both being very loud; also an apex systolic murmur. The heart, as you see, is very much dilated and hypertrophied. The diagnosis was double aortic disease with mitral regurgitation, probably relative. There was no tricuspid murmur. The ordinary treatment was adopted, but there was no great improvement; in fact, the patient slowly got worse. The symptoms were particularly those of lung infarction and anasarca. The latter often required subcutaneous drainage, sometimes as many as ten litres a day being drawn off. The most striking thing was the almost negative response to treatment by rest and medicine. The patient was never bled, because from the beginning he was very anæmic, and the temporary result of tapping the leg was just about as good as I have seen in similar cases from bleeding.

At the autopsy we found the heart as you see it, and the point I want to speak of is the stretching of the auricle in such a way that wide areas are left without muscular tissue at all, only the serous membranes being left. Of

[1] Deutsch. Arch. f. klin. Med., lii. p. 97.

course, it is well known that in loss of compensation the right auricle is extremely dilated in most cases, but we know that in many such cases the auricle can recover its normal size, especially if we bleed the patient; but in a certain number of cases the improvement is only very temporary. In cases somewhat similar to this I noticed four or five years ago that there was a similar condition of stretching of the auricular fibres. This is the third case I have examined, and I have been calling attention in my clinical lectures to the fact, and suggesting that many cases of loss of compensation may be due to the inability to recover proper shape. There was no way to diagnose it, however, except by guesswork; but Dr. Cushny's work seems to offer valuable assistance in such cases. Other conditions, of course, might give rise to the auricular irregular pulse, especially of fibrous degeneration, but, since the article he mentions, published several years ago, I have not been able to find a case in which it was the cause. I think the matter is extremely interesting in connection with the tracings shown and the theory of the auricular irregularity of the pulse, and that observations with the sphygmochronograph may furnish results of value.

In one of the cases I mentioned the history was similar to this, the symptoms being specially marked on the part of the lungs and liver. The man was bled frequently and improved each time, but within a half hour would be in as bad a condition as before the bleeding.

It may be well to add that the auricle as seen here is not artificially distended, but, on the other hand, to a certain extent the fibrous tissue spaces have narrowed by drying.

DR. JACOBI: In the light of what I have just heard I now understand a condition I have frequently observed. It has always struck me that the intermission in the many heart diseases we find, particularly in those accompanied by exhaustion or fatty degeneration, where the intermission is not regular at all, that it was not complete. I understand now why. We are told that an intermission that results from a disease of a ventricle is not complete—that it occupies only one-half or three-fourths of the pulse-length, and that coincides with the fact that auricular diseases are comparatively rare when compared with ventricular diseases. I think the relation must be about the same as the numerical relation of, say, atheromatous degeneration of the arteries, which is frequently compared to that of the veins, which is rare. Whether the proportion is the same or not I do not know; perhaps there are no statistics, but it looks probable.

DR. CUSHNY: Dr. Jacobi has stated that auricular disease is rare, but I cannot discuss this point very well, as my experience has been somewhat limited. In a certain number (about one-half) of the cases which I examined the intermission was auricular, while in the other half it was ventricular. Some of the auricular intermissions may not have been due to disease of the auricle, but may have been inhibitory in nature, but I formed the impression that a very considerable number were due to disease of the auricle. Of course, I made no post-mortem examinations and cannot say positively.

THE ACTION OF HEPATIC, RENAL, AND OTHER CELLS ON PHENOL AND INDOL, UNDER NORMAL AND PATHOLOGICAL CONDITIONS.

By C. A. HERTER, M.D., and A. J. WAKEMAN, Ph.D.,
of New York.

It is the object of this communication to give the results of experimental observations on the behavior of various animal cells toward certain substances belonging to the aromatic type, notably phenol and indol. The inquiry was prompted by the interest which attaches to a study of the natural defences of the organism against various kinds of damage through chemical agencies. Prominent among the problems that arise in connection with such an inquiry are: First, the determination of the seat of the defensive action of the organism, whether chiefly in the blood or in the cells; secondly, the relative activity of the different kinds of cells in the neutralization of the toxic properties of the particular chemical agents employed; and, third, the character of any chemical transformation that may take place when these substances are acted upon by living cells.

Indol and phenol were selected for use in the inquiry for two reasons: First, these substances are normal products of proteid cleavage in the intestine, under the influence of bacteria and of the proteolytic ferment of the pancreatic juice, and they are often formed in excessive amounts in the course of digestive derangements. Greater interest thus attaches to the fate of these substances in the organism than to that of wholly foreign poisons. Secondly, both indol and phenol are recognizable by means of delicate color reactions, and it becomes possible by means of the procedures to be described to make use of these color tests for the purpose of comparing the relative proportion of phenol and indol present in different solutions.

THE CONTACT METHOD.

Two methods were pursued in our observations. In the first, the organs of healthy rabbits were quickly removed, after bleeding nearly to the point of death. After chopping the organs into fine bits, seven

grammes of the pulp of the liver, kidney, brain muscle, and seven grammes of the blood were brought into contact with ten c.c. of a weak solution of phenol and indol of known strength. The period during which these solutions were left in touch with the organ pulps varied in different experiments, two or three hours being the usual period. At the end of this time the mixture was subjected to distillation. The distillate was then tested for the presence of indol by the nitroso-indol test, and for phenol by means of Millon's reagent. By placing in columns equal heights of distillates in test-tubes it becomes possible to arrange these in the order of the intensity of their color. Two or more members of the series sometimes give colors of equal intensity, or the differences may be so small that it is difficult to be certain of any difference. Usually, however, a good gradation of color can be obtained throughout the series. It is hardly necessary to state that the utmost care in technique is necessary in making these observations by what we have come to call the "contact method." Under carefully controlled conditions it is possible to obtain reliable and consistent results. It will be seen by reference to the tables that the different organ pulps possess in different degrees the powers of causing the disappearance of the phenol or indol with which they are brought in relation.

TABLE I.—EXPERIMENTS WITH PHENOL—CONTACT METHOD

No. hours contact.						
3 . . .	Blank	Bn	Bd	M	K	L
3 . . .	"	Bd	Bn	M	K	L
3 . . .	"	Bn	Bd	M	K	L
3½ . . .	"	Bn	Bd	M	K	L
4 . . .	"	Bd	M	K	Bn	L
3½ . . .	"	Bd	M	K	Bn	L
3½ . . .	"	Bn	Bd	M	K	L
3½ . . .	"	M	Bd	Bn	K	L
3 . . .	"	Bn	Bd	K	M	L
3 . . .	"	Bd	Bn	M	K	L
3 . . .	"	Bn	Bd	M	K	L
3 . . .	"	Bd	Bn	M	K	L
3 . . .	"	Bn	Bd	M	K	L
3 . . .	"	Bd	K	Bn	M	L
2 . . .	"	Bn	Bd	M	K	L
21 . . .	"	Bd	Bd	M	K	L
Few minutes .	"	Bn	Bd	M	K	L
6 . . .	"	M	M	Bd	—	L
3 . . .	"	Bd	Bn	M	K	L
2 . . .	"	Bn	Bd	M	K	L
2 . . .	"	Bn	Bd	M	K	L
About 2 hours	"	Bd	Bn	M	K	L
2 . . .	"	Bn	Bd	M	K	L
3 . . .	"	Bd	Bn	K	M	L
3 . . .	"	Bd	Bn	M	K	L
1 . . .	"	Bn	Bd	M	K	L
3 . . .	"	Bd	Bn	K	M	L
3 . . .						

Bd = blood; Bn = brain; M = muscle; K = kidney; L = liver.
The tissues increase in activity from left to right as arranged in the columns above.

That all of them possess some activity is seen by the fact that their distillates yield less color than a blank control of the solution, which has also been subjected to distillation. We may refer first to the results obtained with phenol and then to those with indol.

ORDER OF ACTIVITY OF DIFFERENT CELLS.

Of the twenty-seven observations on phenol it is seen that the liver distillate gave the smallest amount of color in all of the twenty-seven cases—*i. e.*, in all instances the activity of the liver in disposing of phenol was greater than that of any of the remaining organs studied. In the table (I.) in which the organs are arranged in series, according to the color reactions of their distillates, this fact is clearly brought out by the circumstance that all the livers are to be found in the right-hand column. The table shows, further, that the kidney occupies the next place to the liver as regards activity. Of the twenty-six cases in which the kidney was studied it comes into the column next to that of the liver in twenty. In the next column the muscle occurs nineteen times. In the next column to the left the blood is found in fifteen cases. In the next column the brain is found thirteen times. Finally, in the first column are seen all the control observations made upon blank solutions of phenol like those that were used in the contacts. With the exception of six instances it was possible to obtain a gradation of color. Where the blood and muscle gave the same tint this is indicated by a line drawn under the tissues.

Thus it is evident that in all instances the blood, brain, muscle, kidney, and liver exerted some influence in transforming a certain amount of phenol, so that it no longer responds to Millon's reagent. The results show very clearly that in point of activity the liver leads, with the kidney a close second and the muscle third. The blood and brain occupy the fourth and fifth places, although they are both less active than the muscle. The brain and blood are much alike in their behavior and appear to exert little action on the phenol. On the other hand, the action of the liver is often sufficient to yield only a very feeble color reaction with a solution of the strength employed.

Looking now at the results in the case of indol (Table II.), it is seen by the table that here there is less uniformity than in the case of phenol. There are thirty observations in all, but in many of these

a gradation of color through the series is impossible, so that many ties are noted in the table. Taking the liver first, it is seen that there are twelve cases in which it leads in activity. Twice it is tied with the kidney, once with the brain, twice with muscle and brain, twice with kidney and brain, and once with kidney, muscle, and blood. In spite of these ties, however, it is clear that the liver leads the other organs in activity. But the kidney is a very close second, and is found five times in the column indicating the greatest activity.

Without going into further detail, it may be stated that notwithstanding numerous irregularities, the table indicates that the order of activity of the cells acting on indol is as follows: liver, kidney, muscle, brain, and blood. Between the activity of brain and muscle there seems little difference.

In one respect these results differ from those obtained in the case of phenol, the blood shows the smallest action of any member of the series, a degree of activity apparently less than in the case of phenol.

TABLE II.—EXPERIMENTS WITH INDOL—CONTACT METHOD.

No. hours contact.						
2	Blank	Bn	Bd	M	K	L
3	"	Bd	M	K	Bn	L
3	"	Bd	Bn	M	K	L
2	"	Bn	Bd	M	K	L
4	"	Bd	Bn	M	K	L
20	"	Bd	L	Bn	M	K
20	"	Bd	M	Bn	K	L
4	"	Bd	M	Bn	L	K
4	"	Bd	Bn	M	L	K
4	"	Bd	Bn	M	L	K
4	"	M	Bd	Bn	K	L
4	"	Bd	M	K	Bn	L
3	"	Bn	Bd	M	K	L
3	"	Bn	Bd	M	K	L
4	"	Bn	Bd	M	K	L
20	"	Bd	L	Bn	M	K
20	"	Bd	M	Bn	K	L
4	"	Bd	M	Bn	L	K
4	"	Bd	Bn	M	L	K
4	"	Bd	Bn	M	L	K
4	"	Bd	M	Bn	K	L
4	"	Bd	M	K	Bn	L
3	"	Bd	M	K	Bn	L
3	"	Bn	Bd	K	L	M
2	"	Bd	Bn	K	M	L
3	"	Bd	M	Bn	K	L
3	"	Bd	M	Bn	K	L
—	"	Bd	Bn	M	K	L
20	"	L	Bd	Bn	K	M
3	"	Bn	Bd	K	M	L

Bd = blood; Bn = brain; M = muscle; K = kidney; L = liver.

The left-hand columns indicate the least activity on the part of the tissues.

Isolated trials of the activity of the epithelial lining the small intestine of the rabbit indicate that these cells possess a high grade

of effectiveness comparable to that of the liver cells. The cells of the spleen pulp are similarly but somewhat less active. Observations were also made with potato in order to ascertain whether the properties noted in animal cells pertain also to vegetable tissues. The results indicate a moderate degree of activity on the part of potato in transforming phenol. Similar trials with egg albumin showed absolutely no action on the part of the proteid material. Experiments with gelatin gave entirely negative results.

Experiments were made to establish the influence of the time element in the contact procedure. In some instances the duration of the contact was twenty-four hours. The organ pulps subjected to this long exposure showed no greater action than those exposed for only one hour. There is good evidence that the action is normally complete at the end of the hour, and that the greater part of the transformation occurs in the first twenty minutes. Organ pulps protected against putrefactive change show very little diminution in activity even after the lapse of several days.

THE INFUSION METHOD.

The second method employed in the study of the action of the different organs on phenol and indol consists of making intravenous infusions of solutions of those substances. Usually the injections were made until nervous symptoms appeared. The animals were then killed promptly, and definite weights of the liver, kidney, muscle, brain, and blood were subjected to distillation. Color tests were then made on the distillates, so that the quantity of phenol and indol found in the different tissues might be roughly compared. In order to minimize the influence of an admixture of blood with the cell pulps the animals were bled to death.

It is, of course, evident that owing to the time that must elapse between the death of the animal and the beginning of distillation some transformation must go on during the interval, and thus give rise to a source of error in the results. . . . The operations were, however, carried on with the smallest delay, and it does not seem probable that this source of error can seriously influence the results. A review of the results shows that there is much confusion in the order of the color tints. Nevertheless, a certain degree of order can be observed in the gradation of color. The muscle occurs in the right-

hand column in ten of eighteen observations made with phenol, and in three further observations the muscle is tied with the blood or liver. There is thus no doubt that the muscle distillates in these experiments exhibit less color than any other organ. The interpretation of this result is not entirely clear. It may be due to the fact that less phenol has passed into the muscles from the blood, or it may be due to the fact that the phenol entering the muscles is more rapidly transformed than the phenol which goes elsewhere. The results of the contact experiments are perhaps of help in the interpretation of the behavior of the muscle. It will be recalled that these observations showed the muscles to be less active than the liver or kidney. Unless, therefore, we assume that the activity of the muscles is relatively less outside the body than when the blood is passing through them, it appears probable that the muscle takes up less of the phenol than do other organs. According to this view the position of the muscle in the injection experiments would be largely due to their lesser absorption of phenol from the blood.

As regards the position of the kidney, liver, brain, and blood in the phenol injection experiments, it is difficult to establish a definite order in the color results. The liver and kidney in the average of results appear not to differ much. Both show more color than the muscles. This cannot be attributed, in the light of the contact experiments, to an inferior ability to transform the phenol, but is rather due to the greater storage of phenol in these organs during the injection. Finally, the brain and blood show a still stronger coloration than the liver and kidney. This is not surprising, as the contact experiments clearly indicate that the blood and brain are comparatively inactive. In our injection experiments sufficient time has not elapsed for the withdrawal of all the phenol from the blood.

The observations relating to the infusion of indol resemble those with phenol in the irregularity of the results. Certain facts, nevertheless, stand out clearly. In the case of the indol, as with the phenol injection, the muscle is generally found to contain less of the infused substance at the end of the infusion than any other tissue. Here, again, some difficulty arises in interpreting the results. Is the small content of indol due to small absorption or to active transformation into some other substance? Referring to the experiments with the indol contacts, it will be recalled that the muscle exerts less energy in

transforming indol than either the liver or the kidney. Unless, therefore, the absorption of indol were less than in the case of the kidney and liver, the position of the muscle in the series could not be accounted for. It seems probable that the slighter absorption, together with the moderately active transforming power of the muscle, suffices to explain its behavior.

Another fact which deserves comment is the position of the liver in the series. In a very large proportion of cases the liver yielded more color than any other tissue. This striking result can hardly be accounted for except on the ground that the liver is more active than any other tissue in removing indol from the blood. There certainly is no reason to think the liver less active than other tissues, if we can be guided by our contact experiments. Our inference is that the liver takes indol from the blood much more actively than it does phenol. The ability of the liver to dispose of the indol stored up at the end of the infusion is illustrated by the fact that if the animal be not killed until the lapse of twenty or thirty minutes the amount of indol stored in the liver is no greater than that found in the other organs. This fact has been verified by numerous observations.

The following observation has reference to the exceptional behavior of the tissues in an individual animal. It appears of sufficient importance as an example of individual variation on the part of the cells to be mentioned here. A rabbit weighing 1900 grammes received an infusion of saturated indol solution at the rate employed in other observations. Before the injection was begun the animal seemed unusually nervous. After the injection was begun, spasm came on early and the pupils became very small. The irritative symptoms soon wore away, but the animal continued restless. The total amount of the infusion was 28 c.c. The animal died half a minute after the close of the injection, and was bled from the heart. The striking peculiarity in the behavior of this animal during the infusion was that the nervous symptoms, spasms, contracted pupil, and restlessness came on much earlier than is usual. Another peculiarity of the animal was the readiness with which the muscle substance could be torn.

On studying the organs in reference to their contents of indol, it was found that the kidneys, the liver, and the muscle contained only the smallest traces of indol. The blood and the brain, on the other

hand, contained a large amount of indol—that is, they yielded a strong color reaction. This behavior on the part of the various tissues is quite without parallel in our experience. It is evident that in this case the liver, kidney, and muscle were unable to remove indol from the blood with the usual promptitude. The brain, on the other hand, took out a larger amount than is usual, and one is tempted to connect the very pronounced nervous symptoms observed in this animal with the relatively large quantity of indol found in the brain. It also seems likely that the inability of the liver, kidney, and muscle to remove the poison from the blood was dependent on some constitutional peculiarity.

NATURE OF THE ACTION EXERTED BY THE CELLS.

In the course of the preceding pages reference has repeatedly been made to the activity of the liver, kidney, muscle, etc., in effecting the transformation of phenol and indol. What is the nature of this transformation which leads to the disappearance of a portion of the phenol and indol brought into relation with the living cells? This question, which has a high degree of biological interest, cannot at present be satisfactorily answered. There are, however, certain facts relating to the subject which may be briefly considered here.

In the first place, it is clear from the observations cited that the processes by which phenol and indol are altered are carried on much more actively in the cells of the liver and kidney, and probably also in those of the muscle, than those of the blood. The property of effecting these changes is unquestionably inherent in the cells themselves, and the transformation in the organism must occur in the blood in comparatively slight degree.

This fact is in accord with the teaching of modern physiology in reference to the seat of the oxidative changes that occur within the body during life.

In recent years several investigators have devoted attention to the nature of the oxidizing processes that are carried on in the cells. The methods and results of certain of these observers show some resemblance to the methods and results that have been referred to in this paper.

Jaquet[1] appears to have been the first to make observations as to

[1] Ueber die Bedingungen der Oxydations vorgänge in den Geweben, Arch. f. Exp. Path. u Pharmak., 1892, Bd. xxix. p. 386.

the occurrence of oxidative processes in cells that have been removed from the body. He found that in lungs cut out of the body, one gramme of benzyl alcohol added to blood circulating experimentally through the organs was oxidized and yielded 185 mgr. of benzoic acid. Jaquet found that the oxidation was as complete if normal salt solution, instead of blood, was employed as the circulating fluid. Moreover, he found that the tissues of the horse (kidney and muscle) were active even after immersion in 80 per cent. alcohol for fourteen days, and that an extract of fresh or alcohol hardened tissue in salt solution possessed good oxidizing powers. These, however, were lost by boiling.

Jamagawa,[1] a pupil of Salkowski, soon confirmed the results of Jaquet. He found that different tissues were active in the following order of decrease: (1) Spleen, (2) liver, (3) kidney, (4) pancreas, and (5) muscle. Then Spitzer[2] found that extirpated tissues generally have the power of inducing certain oxidative syntheses—for example, the synthesis of naphtol and paraphenyl diamine to form an indophenol. In recent papers Spitzer[3] attributes the oxidative action of the cell to its nucleo proteid. He finds that certain constituents of the proteid molecule, such as histon, also possess the oxidative power, and reaches the conclusion that the presence of iron is essential to these activities.

Salkowski,[4] in his more recent work, concluded that the ferment whose action is noted in the case of cells removed from the body cannot be identical with the oxidizing ferment of living cells, because they do not oxidize certain substances which are readily converted in the living body. This is true, for example, of the oxidation of phenylpropionic acid to benzoic acid. Such evidence as we now possess certainly indicates that the oxidative changes carried on by cells removed from the body have reference to substances that are readily oxidized. Thus the conversion of benzyl alcohol to benzoic acid, of salicylic aldehyde to salicylic acid, of arsenious to arsenic acid, of benzol to phenol, of formic aldehyde to formic acid, are all examples of com-

[1] Ueber das Oxydations ferment der Gewebe. Centralbl. f. de med. Wochenschrift, 1894, p. 919.

[2] Die Zuckerstörende kraft des Blutes und der Gewebe. Pflüger Archiv, 1895, Bd. lx. p. 303.

[3] Die Bedentung gewisser Nueleoproteïde für die oxydative Leistung der Zelle. Pflüger's Archiv, 1897, Bd. lxvii.

[4] Fur Kentniss der Oxydations ferment der Gewebe. Virchow's Archiv, 1897, Bd. clxvii.

paratively readily induced oxidation. We are as yet unjustified in holding that such changes go on with equal vigor in cells outside the body and in the fully living cells. Similarly, with reference to syntheses, there are certainly some which the removed cells cannot perform. Spitzer was unable to confirm the statement that the synthesis of urea from ammonium salts can be made to occur outside the body. Our work with indol indicates that the synthesis of indoxyl potassium sulphate cannot be accomplished by extirpated cells. It also seems improbable that the dead cells convert phenol into phenol-sulphuric acid. Yet we know that these syntheses are performed in the organism, probably by the very cells which fail to effect them outside the body. It is natural to ask whether the known oxidative activities of the dying cells, to which reference has already been made, are the same activities that lead to the disappearance of phenol and indol during contact experiments.

The order observed by Spitzer, Salkowski, and others in the activity of the different cells outside the body agrees closely with the order observed in our contact experiments with phenol and indol. This fact suggested that the changes observed in the case of phenol is in the nature of an oxidative transformation. The oxidation of phenol leads to the formation of pyrocatechin and hydroquinone, substances which are met with in the urine under certain conditions of disordered metabolism. With a view to determining experimentally whether such a transformation goes on in the case of phenol when this is brought into contact with fresh cells, ten kilos of ox liver were reduced to a fine pulp and brought into contact with a solution of phenol and subjected to the contact procedure which has already been described. After a sufficiently long period of contact an endeavor was made to isolate any pyrocatechin or hydroquinone which might have been formed during the period of contact. It was found impossible to recover either of these substances. With the method employed it would have been possible to recover these bodies had they been present in even smaller quantity than might be expected from the action of so large a bulk of liver cells upon phenol. The negative results obtained indicate that the disappearance of phenol, which occurs after contact with liver tissue, does not depend upon a process of oxidation into either dihydroxyl or benzene. This conclusion is supported by the fact that phenol introduced into the circulation leaves the body ordi-

narily as phenol sulphuric acid and not as hydroquinone or pyrocatechin.

In the case of indol, it is thought that the first transformation that occurs in the organism is a process of oxidation into the indoxyl radical. It is possible that this oxidation occurs in the liver, but this is by no means certain. If this be the case the action of the cells is perhaps comparable to the oxidative processes that have been studied by Spitzer and others. In what follows no further reference will be made to the fate of indol when acted upon by living cells. Attention will be confined to the discussion of the action of the cells upon phenol, an activity which apparently belongs in another category from that displayed toward indol.

The view held by Spitzer, Salkowski and others, that the oxidation which occurs through the action of cells is dependent on the presence of a ferment, raises the question whether such an agency will explain the behavior of cells toward phenol. The following facts bear directly upon this problem: Seven grammes of liver reduced to a pulp were brought into 75 c.c. of absolute alcohol for one hour. The usual amount of phenol was then added to the liver pulp, and after a time subjected to distillation. The activity of the liver was slightly, but only slightly, impaired. In another experiment the usual amount of liver was boiled in 50 c.c. of distilled water and then brought into relation with phenol. Only the slightest falling off was noted in the action of the liver. In another case the liver was exposed to hot air, the temperature of the oven being gradually brought to 170° C., and kept there for twenty minutes. On exposure to the action of phenol the liver showed no appreciable reduction in activity. Again, seven grammes of liver were boiled with water, filtered hot, boiled again with water and filtered, and then boiled a third time and filtered. The pulp remaining on the filters showed itself capable of acting upon phenol with only a slight diminution in power. A test of the watery extract of the liver showed that it exerted only a very slight influence on phenol. Other trials made, by bringing 10 c.c. of bichloride of mercury into relation with seven grammes of liver, showed that this procedure only slightly diminishes the activity of the cells.

Similar observations made with a 50 per cent. solution of concentrated sulphuric acid yielded the same results. A 10 per cent. solution of nitrate of silver was entirely without effect. In the case of the

experiments with bichloride of mercury, sulphuric acid, and nitrate of silver, the time of exposure of the liver cells was one hour.

In view of the facts just cited, it appears in the highest degree improbable that any considerable ferment action can be attributed to the liver cells in connection with their behavior toward phenol. Another consideration which harmonizes with this conclusion, is the fact that it is possible to completely exhaust the activity of the liver cells by repeated exposure to the action of phenol.

Although no wholly satisfactory explanation can be advanced as to the nature of the phenomenon under discussion, one is led to speculate whether we have not to deal with some loose combination of the phenol molecules with the molecules of the cell-substance. That the combination between the cells and the phenol is a loose one is suggested by the fact that phenol absorbed from the intestine or injected into the circulation reappears in the urine as phenol sulphuric acid.[1] It would also appear that the protoplasm of the cells suffers no damage when exposed to the action of phenol within physiological limits. The product formed by this combination of phenol with the cell-substance may perhaps be likened to some of the numerous addition products known to chemistry.

The belief that the combination of phenol with the living protoplasm of the liver cells is a loose one harmonizes well with the rapid elimination of phenol following the introduction of this substance into the circulation. It is obvious that it would be advantageous to the organism for phenol to be temporarily held by the hepatic cells while the neutralization of the poison through combination with sulphuric acid is taking place. The manner in which such an arrangement would protect the nervous system, which is highly sensitive to the action of phenol, is sufficiently evident.

One other fact deserves mention in this connection. This has reference to the view advanced by Loew, that phenol acts upon living protoplasm by entering into combination with the labile groups which

[1] The phenol which enters the organism leaves the body almost quantitatively in the form of phenol, as is well shown by the following experiment: Into a large rabbit 0.080 gramme of phenol in watery solution was injected intravenously. The urine was collected for twenty-four hours, and the phenol contained in the urine was determined by means of the iodine and sodium thiosulphate method. The quantity of phenol recovered was 0.0817 gramme. It is possible that a few milligrammes of this phenol were derived from the intestine of the animal. The observation indicates, however, that the greater part of the phenol introduced was recovered.

it contains, and especially groups possessing an aldehyde structure. With a view of testing this hypothesis the liver cells were subjected to the action of solutions of hydroxylamine, which enters readily into combination with aldehydes. Liver pulps treated in this way showed themselves to be as active or nearly as active in the conversion of phenol as normal livers.

In conclusion, the opinion may be ventured that whatever may ultimately be learned of the nature of the phenomenon under discussion, it is likely that the capacity to act upon phenol which cells possess is only one expression of a function that can be exerted upon numerous allied aromatic substances, and it is possible that a similar action may be exerted upon non-aromatic bodies.

ACTION OF HEPATIC CELLS UNDER PATHOLOGICAL CONDITIONS.

As already mentioned, the degree of action exerted by the liver cells upon phenol and indol is fairly uniform. This fact suggested the possibility of recognizing alterations in the capacity of the liver cells to transform these substances under pathological conditions. It was therefore determined to make a series of studies of the liver cells of animals which had been subjected to different pathological influences. These observations include a study of the effects of prolonged anæsthesia, of poisoning by ricine, alcohol, morphine, etc., and of staphylococcus infection.

It is clear that it is a matter of considerable theoretical interest to know whether a definite impairment of functional activity in the cells of the liver and kidney is bound up with pathological influences like these just named. Efforts were therefore made to reach a decision upon this question, although the difficulties attending these efforts were found to be somewhat discouraging.

The chief difficulty arises from the fact that the differences between the action of the normal and of the pathological tissues are not great. This is what might have been expected, in view of the existence exerted by cells to the action of sulphuric acid, alcohol, etc. In order to establish the existence of such slight variations from the normal, it was found necessary to exercise great caution in making comparisons between the distillates from the normal and the presumably pathological organs. It was soon found that the difference in the action of the kidneys and

muscles was usually so slight in the pathological cases as compared with the normal that no inferences could be made. Only in the case of the liver, the organ where action upon phenol and indol is the most energetic in conditions of health, was it possible to obtain satisfactory results.

The distillates from the livers of pathological animals obtained through the "contact method," already described, were compared not merely with individual distillates from the liver of normal animals, but also in many instances with mixtures of the distillates of the liver from many different animals. Great care was taken to make the conditions of the experiments the same as regards freshness of the organs, duration of the contact, quantity of distillates, and the amount of reagent added to give the color, etc.

ANÆSTHESIA BY ETHER AND CHLOROFORM.

The observations upon ether and chloroform included fifteen cases in which ether was used for anæsthesia and nine cases in which chloroform was employed. Of the fifteen cases of anæsthesia the liver cells were brought into contact with phenol in eleven, with indol in four. Of the nine cases of chloroform anæsthesia, the livers were subjected to the action of phenol in four cases and to that of indol in five.

The rabbits subjected to etherization were kept under the influence of the anæsthetic for periods varying from five minutes to five hours in different cases. Although in four of the nine instances in which phenol contacts were made the liver did not show the greatest activity of any member of the series, in the remaining cases the liver maintained its place as the most active organ. In most instances, however, the transformation of phenol was distinctly less than that effected by normal livers employed as controls. A similar difference was noted in the case of three of the four indol-contact observations. In the fourth case, where the animal had been under ether for two hours and a quarter, the brain, blood, liver, kidney, and muscle showed very slight differences in activity, and the inference seems warranted that the activity of the liver, muscle, and kidney are all below the normal.

The observations upon chloroform anæsthesia give even more definite results than those with ether. In two of the four cases where phenol was used (the animals being anæsthetized for three hours) the liver gave evidence of lessened activity. In the two remaining cases

the liver, muscle, and blood showed little or no difference in activity, a condition indicating that both liver and muscle were less active than normal. In four of the five observations with indol the liver was distinctly less active than the normal controls. In the fifth case the result was just the reverse.

Taking the results of these experiments with anæsthesia, as a whole, there can be no doubt that the prolonged action of chloroform and of ether depresses the activity of the liver in the conversion of phenol and indol. In exceptional instances it is not possible to detect this influence, but the exceptions are so few that they do not affect the general result.

POISONING BY ALCOHOL.

Ten observations were made upon rabbits which had been subjected to the action of subcutaneous injections of 25 per cent. alcohol. The periods of intoxication varied from a few hours to four days. The dose of alcohol was large in every instance, and the animals were well under the influence of the poison. Thus in several cases the animal received 160 c.c. of 25 per cent. of alcohol in three days, and lay in a stupor most of the time.

Two of the ten observations were made with indol, eight with phenol. The periods of contact were varied from two to twenty hours in certain instances, the other conditions of the experiment being kept the same, but no differences in results were detected which were referable to the differences in the length of contact. In a few cases the activity of the liver was less than that of the normal controls, but more often no distinct falling off from the normal could be detected. Although we are not prepared to state that acute intoxication from alcohol is wholly devoid of effect upon the liver's action on phenol, our observations make it likely that there is either no influence of this kind or that it is very slight.

POISONING BY RICINE.

Thirteen trials were made to determine whether ricine poisoning exerts any influence on the ability of the liver to dispose of phenol and indol. It was thought probable that such an influence would be discernible, as ricine has been shown to cause well-defined histological changes in the liver, kidney, etc. The dose employed was, unfortu-

nately, too large (0.001 gramme to the kilo), and the duration of the poisoning was too short (less than thirty hours) to develop the degenerative lesions referred to. The results in the thirteen cases were negative.

POISONING BY AMMONIUM CHROMATE.

Observations were made upon four rabbits poisoned with ammonium chromate. The animals received two doses hypodermatically of 0.025 ammonium chromate, and were killed on the third day. The behavior of the liver cells did not positively differ from that of normal cells subjected to the same processes of contact with phenol and indol previous to distillation.

STAPHYLOCOCCUS INFECTION.

The influence of staphylococcus infection was studied in two cases. The rabbits received 5 c.c. each of a culture of staphylococcus pyogenes aureus grown two days in bouillon. The organism was obtained from a patient with follicular tonsillitis. The animals were permitted to live one week, during which time they lost considerable weight. They were then killed by bleeding and the tissues subjected to the usual procedure. In both cases the differences in the activity of the brain, blood, muscle, kidney, and liver were less than is usual in normal series. The distillate from the livers in the two cases was more colored than is usual in the case of normal livers.

These observations appear to indicate that in staphylococcus septicæmia there is some impairment of the activity of the liver and kidney, but they can hardly be looked upon as conclusive.

MORPHINE POISONING.

Eight observations were made upon rabbits under the influence of morphine. The animals received from five to eight grains of sulphate of morphine. Some of the animals lived only a few hours; others lived as long as two days. In four instances the activity of the liver, as compared with that of normal controls, was apparently somewhat lessened, but the deviation from the normal state was very slight. In every case except one the muscle showed greater capacity for transforming phenol than did the normal muscle. In several instances the difference was considerable, as indicated by the color reaction. In

several instances the kidney also showed an apparently increased activity.

DOUBLE NEPHRECTOMY.

In five instances a double nephrectomy was performed, with a view to seeing whether the removal of the kidneys is instrumental in impairing the activity of the liver. The animals were killed in from twenty-two to twenty-four hours. In all cases the liver showed a slight falling off in activity as compared with normal controls. The muscle and kidney, as in the case of morphine poisoning, showed in all cases somewhat greater capacity than usual, but the difference was slight.

INFUSION OF 1 PER CENT. ACETIC ACID SOLUTION.

With a view to learning whether a reduction in the alkalinity of the blood has any influence upon the liver, a 1 per cent. solution of acetic acid in a 1 per cent. solution of sodium chloride was infused intravenously at the rate of 5 c.c. per minute. The animal (a medium-sized dog) went into coma before the completion of the infusion, which consisted of 130 c.c. The animal excreted no urine during the period of injection. It was found that the activities of the liver, brain, and muscle were about the same and distinctly inferior to the action of the kidney. A similar relationship has not been observed in normal dogs, and it seems probable that the infusion of acid distinctly reduced the activity of the liver.

A similar observation with acetic acid conducted on a large rabbit gave a result comparable to that just noted in the case of the dog.

BENZOIC ALDEHYDE POISONING.

In these instances a saturated solution of benzoic aldehyde in water (1 part to 30) was infused into the venous circulation at the rate of 5 c.c. per minute until the animals died after developing symptoms of poisoning. The quantity of the solution infused varied from 80 c.c. to 210 c.c. in the different cases. The livers from these rabbits showed some falling off in relation to their action on phenol. It was found, however, that the benzoic aldehyde employed in the experiments gave a slight reaction with Millon's reagent, and it is therefore possible, though not probable, that the abnormal behavior of the liver de-

pends on the presence of phenol in the benzoldehyde in addition to the phenol added in the course of the contact procedure. It is to be regretted that this source of error exists, as it would be interesting to know whether the exhaustion of the oxidative activity of the liver upon a readily oxidized substance like benzoldehyde necessarily causes impairment of the ability to transform or bind phenol.

INFUSION OF UREA.

Infusions of urea were made in several instances, with a view to overworking the kidneys and observing whether such overwork causes any impairment in the activity of the kidney in converting phenol. The results obtained were wholly negative.

In addition to the various experimental observations recorded above, a number of trials were made upon fatty and cirrhotic livers from human subjects. Owing to the delay incidental in obtaining human material after death, it was impossible to obtain satisfactory results. It may be stated, however, that no marked deviations from the normal capacity of the liver to convert phenol were observed in organs the seat of the most advanced structural alterations.

It is probably safe to conclude that no pathological conditions which can be induced in the liver during life are capable of destroying or even of markedly reducing the capacity of the liver cells to act upon phenol and indol.

THE ORGANISM IN A CASE OF BLASTOMYCETIC DERMATITIS.

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SINCE the description by Gilchrist, in 1894, of blastomycetic dermatitis, and the report by Gilchrist and Stokes[1] of the second case, two more instances have been recorded—one by my assistant, H. G. Wells,[2] which, like the two previous cases, resembled lupus vulgaris clinically, and the other and fourth by R. Hessler.[3] The latter's case began as a pimple, which gradually enlarged and formed a small abscess, from the contents of which a blastomyces was cultivated. After evacuation the abscess healed, but at the time of the report new foci were making their appearance in the neighborhood of the old scar. The only other of the four instances of blastomycosis of the skin in which the organism has been isolated in pure culture is that of Gilchrist and Stokes, who record full observations on the cultural, morphological, and pathogenic properties of the blastomyces dermatitidis, which is the name they gave the fungus in their case.

It is now proposed to describe briefly the results of the histological and biological examination in the case of blastomycetic dermatitis recently under the care of Professors Hyde and Bevan, in the Presbyterian Hospital, of Chicago, so as to add to the number of instances illustrative of the action of pathogenic blastomycetes, micro-organisms which of late are attracting considerable attention.

I am under many obligations to Professor Hyde, who saw the case first and referred it to Professor Bevan, for the privilege of making the following abstract of the clinical history:[4]

[1] Johns Hopkins Hospital Reports, 1896, vol. i. 269; Johns Hopkins Hospital Bulletin, July, 1896; Journal of Experimental Medicine, 1898, vol. iii. p. 53.

[2] New York Medical Journal, March 26, 1898.

[3] Indiana Medical Journal, August, 1898.

[4] The clinical aspects of this case are fully dwelt upon in an article by Hyde, Hektoen, and Bevan: A Contribution to the Study of Blastomycetic Dermatitis, British Journal of Dermatology, 1899, xi. In this article occurs also a brief report of a new case of blastomycosis of the skin of the leg, which I found in a museum specimen.

R. B., by occupation a day laborer, aged fifty-six years, married, presented himself for treatment September 20, 1898. He was a native of Holland; at eighteen years of age he left for the East Indies, where he entered the Dutch army, serving in the East. He was then taken ill with some form of fever, which resulted in his leaving the East Indies for his native land. He remained in Holland for eight or nine years after, and came to America in 1892.

His present malady began four years ago by the development of a small reddish spot on the right leg, the disorder gradually extending over its anterior face. For this trouble he underwent an operation in the Dearborn Hospital; he was also treated at the Hahnemann Hospital. The result was the production, in the region named, of a thin, broad, cicatriform tissue, insensitive, and in places scaling.

One year ago the left thumb and wrist were found to be involved in some morbid process, which produced, by gradual extension from the point of original implication, a reddish patch, well-defined in outline, with a bluish-red areola, and a decidedly verrucous aspect. This patch furnished a moist and sticky exudate. The subjective sensations were a sense of soreness and burning, at times decided pain and pricking sensations. The pain often radiated up the arm, so that both the elbow and shoulder of the affected side became sensitive.

The fingers became partially flexed toward the palm; the little finger was thus permanently flexed.

He suffered from headaches, which were frequent and severe; from constipation, and from inappetence. His sleep was poor. His height was five feet, nine inches; weight ninety-eight pounds, a decline from his average weight of one hundred and forty-five pounds. He used tobacco in moderation, but no alcoholic stimulants, though he had once been a heavy drinker.

His father died at the age of ninety-two years, in good health, and his mother at forty-five years, of consumption. There were three brothers living, one dead from consumption; three sisters were dead of consumption, at twenty-one, sixteen, and forty-eight years of age, respectively. He had had six children; four were living and in good health; two were dead, one at thirty-nine months, the other at two and one-half years, from causes unknown.

When examined by Professor Hyde the region of involvement of the right leg extended in an irregular oval, its long axis parallel with the

axis of the extremity, from the lower margin of the upper third of the anterior surface of the limb quite to the lower border of the lower third, its lateral wings barely perceptible when the posterior surface of the leg was viewed from behind. The encroachment upon the calf was about equal on the two sides, the outer wing slightly more elevated than its fellow. This entire surface was covered with a thin, papery substitute for the normal epidermis, which furnished a slight scale.

The dorsal aspect of the proximal phalanx of the right thumb and of the wrist, with a portion of the posterior face of the lower third of the forearm, were involved in a single connected patch of morbid tissue, dull reddish in hue, sharply defined in outline, and having a peculiar bluish-red border extending about 4 mm. away from the edge of the affected area. The body of the patch was made up of an elevated mass of infiltration, with a verruciform development of fine, pinhead-sized papillæ projecting externally, and moistened by a glutinous secretion. Individual elements of this warty growth were readily distinguished by the eye. The palm was completely spared. There was entire absence of other lesions, such as pustules, vesicles, crusts, or the scar-like tissue exhibited on the leg. No other signs of disease were discovered.

For the purpose of further examination and study of the lesion presented by the patient, he was placed in the Presbyterian Hospital, under the charge of Professor Bevan, who, on September 27, 1898, excised a small piece from the upper margin. Frozen sections, stained with hæmatoxylin and eosin, showed extensive epithelial proliferations and cell infiltration in the corium ; in the new-formed epithelial masses were numerous miliary abscesses, in one of which were two round bodies composed of an outer bluish membrane, an inner colorless and hyaline layer, and faintly stained granular contents, with a few blue bodies like cocci. A diagnosis of blastomycetic dermatitis was accordingly made.

Soon afterward Professor Bevan placed the patient on the iodide of potassium, with the result that material diminution in the size of the patch occurred, and such marked amelioration of all the symptoms that the question of operative interference was for the time set aside. The patient had been taking the drug named before he first came under Professor Hyde's observation, but, probably, not in such doses as those administered at the hospital.

MICROSCOPICAL EXAMINATION. Portions of the bit of tissue excised September 27th were fixed in absolute alcohol. On October 6th Professor Bevan, at my request, excised a long, narrow strip from the centre of the lesion on the back of the hand, the clinical appearance of which now indicated rapid healing, especially at the margin. Pieces from this strip were fixed in absolute alcohol, sublimate, and Zenker's fluid. Paraffin sections were stained with hæmatoxylin and eosin, Gram's method, preceded by carmine, and alkaline methylene-blue, with or without counter-stain with eosin.

The histology of the skin lesion may be summarized as follows: It can be said at the outset that the histological appearances in this case are identical with those described by Gilchrist and by Wells. In fact, their descriptions would answer very well for this case also.

The surface of the skin is covered by a horny layer of varying thickness, together with débris, polymorphonuclear leucocytes, blood disks, and bacteria, especially bacilli that take Gram's stain. In places small abscesses have broken through the horny layer, which lies directly on the granular or prickle layer. The striking feature in the sections is the great hyperplasia of the epithelium, very similar to rapid carcinomatous proliferation, and in the form of variously shaped and branching downgrowths of from 3 to 5 mm. in extent, which start from the interpapillary processes principally and cause great distortion of the papillary layer. In the larger columns of epithelial cells the central parts may show degeneration as well as distinct hornification. Isolated epithelial whorls, more or less completely hornified, also occur. The epithelial proliferations are generally separated from the fibrous tissues of the corium by quite a distinct layer of cylindrical epithelial cells, next to which occur typical prickle cells. Occasionally karyokinetic figures occur in the epithelial cells.

Scattered throughout the entire epithelial portion are polymorphonuclear leucocytes, which occur between as well as within the cells. Numerous focal collections of leucocytes, which, when larger, form miliary abscesses, are found in all parts of the thickened epithelium, in the deep prolongations, near the surface as well as directly underneath it, and at times they have broken through externally. The contents of these characteristic abscesses consist of leucocytes, with more or less nuclear fragmentation, desquamated epithelial cells, detritus of horny material, red blood-corpuscles, and the organism

peculiar to the process; in some are also multinuclear giant cells of the tuberculous type. The epithelial cells around the abscesses seem to play an entirely passive rôle and to be flattened out by the pressure of the abscess contents.

The connective tissue between the epithelial down-growths presents typical acute and subacute inflammatory changes; the vessels are congested, leucocytes are seen in the act of migration, and there are hemorrhagic extravasations as well as œdematous districts. The cell infiltration is marked in many places, but there are but very few miliary abscesses, and no organisms have been found in the corium; a few giant cells are present; endothelioid cells, plasma cells, and polymorphonuclear leucocytes make up the principal part of the infiltration; the mast cells are rather numerous. In places young connective tissue has formed. Occasional typical hyaline bodies, mostly as mulberry-shaped masses, are present. In one instance a large cell with a nucleus like that of plasma cells was filled with small hyaline spheres.

As to the appendages of the skin present, it would seem that they play but a passive rôle; the cells of the sweat glands are crowded apart by the inflammatory infiltration, and the hair follicles are the seat of a marked hyperkeratosis.

The organisms in this case do not seem to be present in the tissues as numerously as in the cases previous reported. This impression is gained after carefully looking over a large number of sections from various parts of the area involved. All the mature organisms seen occur in the miliary abscesses in the epithelial proliferations (Figs. 1 and 2), most often singly, sometimes in groups of from two to four; they are invariably situated outside of the cells; not even the giant cells in this case contain any parasites. The parasites, when not budding, are round or oval, and about 10 to 12 mikrons in diameter; they are surrounded by a homogeneous capsule, from which the finely granular protoplasm is separated by a clear zone of varying width; in some the protoplasm contains a vacuole of varying size, which, in a few instances, occupies the larger part of the cell, crowding the granules closely together inside the clear zone, which becomes indistinct; in a few organisms the outer capsule contains oblong thickenings. Budding bodies in varying stages are present; the granular protoplasm pushes the capsule and clear zone before it, forming an

oval bud which grows larger and eventually separates from the mother organism. Methylene-blue gives the best stain of the parasite, the capsule assuming a deep blue color, the protoplasm a lighter blue. There are no red granules in the parasites when stained in this way, as described by Gilchrist.

CULTURES.[1] Smears of soft material from the bit of skin first excised contained a few bacilli and a very small number of round bodies similar to those found in the sections. Three glycerin-agar and three blood serum tubes were inoculated. The resulting colonies consisted of a bacillus mixed with a few large, round bodies; attempts at isolation of the latter by means of the plate method failed. Two attempts at cultivating yeasts from the hand yielded pure growths of a pathogenic bacillus which belongs in the pseudo-diphtheria group. Numerous cultures were also made from the strip of skin removed October 6th; small pieces of tissue were rubbed over the surface of potato, glycerin, and glucose-agar; inoculations were also made in Pasteur's fluid. After twenty-four hours there was a heavy growth upon all the solid media, consisting of a comparatively few large, clear bodies and bacilli. Isolated by the plate method the bacilli proved to be pseudo-diphtheria bacilli already found and an unidentified bacillus; the plates also showed some colonies which consisted of round bodies of variable size; in the subcultures these bodies were so closely and constantly associated with small coccus-like organisms that for a time grave doubts were felt as to the purity of the growth. In subcultures on glycerin and glucose-agar there were noticed, after several days, colonies with two distinct shades of color, namely, a creamy-yellow and an almost pure white. Now, from the yellow part the smears showed only small, round, or oval, often apparently budding, and deeply stained organisms, often not larger than large cocci, while the white colonies consisted of much larger, mostly quite clear, round bodies, varying in diameter from 7 to 10 mikrons.

Inoculations of the smaller organism in the yellow colony on fluid media was followed in two or three days by the growth of a fine film on the surface, which consisted of small bodies, while the slight deposit at the bottom contained mostly larger forms. Inoculations on bouillon with the larger form gave the same results. Cultures of

[1] I am indebted to Mr. H. E. Davies for the successful isolation of the blastomyces in pure culture.

the smaller organisms on glucose- and glycerin-agar at room temperature developed both forms, smears showing long chains of more or less deeply stained small bodies which were closely connected, and at one end of the chain there would often be one or more of the large, clear organisms. It was also soon noticed that when a culture of the larger form became dry the organism seemed to gradually become smaller. It was therefore concluded that it concerned one and the same organism, which in the course of artificial growth appeared in various sizes.

This organism grows readily on all of the following media, the extent and rapidity of growth corresponding roughly to the order in which they are named, beginning with the most favorable: beer-wort agar, glucose- and glycerin-agar, Loeffler's blood serum, potato (alkaline), glucose- and glycerin-broth, lactose-, dextrose-, and saccharose-broth, agar-agar, gelatin, milk, and Pasteur's fluid.

Agar and Gelatin Plates. On glycerin-agar plates pin-point sized and even larger colonies develop in twenty-four hours at 35° C.; they are roundish and oval, rather coarsely but evenly granular and very light grayish in color. With a moderate magnification the individual yeast bodies are readily distinguishable, especially at the margins, where budding forms often occur (Fig. 3, Plate I.). As the colonies become larger the central part turns more opaque; the surface colonies are larger than the deep.

The deep colonies on gelatin plates show the individual, clear, circular bodies very distinctly, while the surface growths are smaller, irregular in outline, more opaque, and composed of much smaller organisms. In the hanging drop colonies of gelatin small, opaque buds are seen between the large, clear organisms. Generally the process of budding results in the growth of small, round colonies, but sometimes peculiar long outgrowths of two or more quite parallel rows of bodies develop, so that the colony becomes more or less club-shaped.

Hanging drop cultures of bouillon show the multiplication by budding very well, and also the structure of the organism (Fig. 4, Plate I.).

Agar. The organism grows most luxuriously upon 5 per cent. beer-wort-agar. On slanting wort- and glycerin-agar there develops in twenty-four hours an extensive grayish- or yellowish-white growth, without any special characteristics, and which spreads itself over the surface, and, especially in the case of the beer-wort-agar, gradually

creeps in between the medium and the glass. With time the growth becomes perhaps more purely white; it remains quite soft and smooth on the surface. In from eight to fourteen days quite abundant, fluffy and feathery masses have grown down into the agar from the under surface of the superficial growth; this is more marked on the beer-wort-agar. These peculiar feathery or downy outgrowths are roundish or cone-shaped, the large ones being as much as 3 mm. in diameter; they are very much like the down-growths characteristic of many varieties of streptothrix.

In stab-cultures the surface is soon covered by a spreading, slightly raised smooth layer. The growth along the needle track becomes quite thick, and presents irregular, nodular, sometimes almost polypoid protuberances which give it a peculiar twisted appearance. In a few days this knobby trunk presents delicate lateral branches springing from various parts of the circumference and passing out into the medium at right angles to the stem, after the fashion of the branches of certain trees. These feathery, often extremely fine, lateral outgrowths resemble very much the tree-like branchings of stab-cultures of many forms of streptothrix.

On agar-agar the organism produces a rather light yellowish-brown pigment which smears show is in the form of small granules that occur about and upon some of the larger clear bodies. This property of pigment production is not observed upon any other media, and develops to a moderate degree on transplantation upon plain agar from whatsoever other medium it may be, but it is not absolutely constant.

Gelatin. The growth on gelatin is rather scanty. There develops a flat, thin, pearly surface layer and an irregularly granular tapering growth along the needle track, with peculiar lateral outgrowths consisting of delicate tufts, straight or branching threads of varying length and thickness; some of the threads break up into an extremely fine terminal network at some distance from the main stem. Gelatin is not liquefied.

Serum. On Loeffler's serum the growth is quite extensive.

Potato. On alkaline potato there forms in twenty-four hours a slight yellowish-white, raised growth of considerable extent; with time this increases materially, the margins being rounded and irregularly wavy. On acid potato the rate of growth is much slower.

Bouillon. In bouillon there forms a granular, rather coarse, some-

times a little stringy sediment, and gradually small granular masses appear scattered throughout the fluid, which at first is quite clear. Sometimes a clear film develops on the surface.

Milk. Moderate growth occurs in milk, without any change in reaction and without caseation.

Fermentation Tests. The organism grows fairly well in the aërobic bulb of fermentation tubes containing lactose-, dextrose-, and saccharose-bouillon, made from sugar-free bouillon, prepared according to Theobald Smith's formula, but without fermentation. It also grows to a limited extent in Pasteur's fluid. It does not produce indol.

Reaction to Oxygen. The organism does not grow in Buchner's jars.

Temperature. The thermal death-point is 54° C.; an exposure to this temperature for two minutes kills the organism. It is not killed by freezing; cultures exposed to a temperature just above zero for two weeks and then frozen solid for two weeks, on inoculation gave rise to typical new colonies.

Relation to Potassium Iodide and the Pseudo-diphtheria Bacillus. The rapid improvement of the local lesion under the use of iodide of potassium suggested the advisability of determining the effect if any of the presence of this drug in the media inoculated. It was found that a 1 per cent. iodide of potassium bouillon furnishes just as favorable a medium for the growth of the organism as ordinary broth.

It also occurred to us that possibly the mixed infection with the pseudo-diphtheria bacillus referred to might play some rôle in the rapid healing of the lesions. The blastomyces was found to grow unhindered in the presence of the bacillus in the same media; it develops just as rapidly in filtered two weeks-old bouillon cultures of the pseudo-diphtheria bacillus as in the ordinary broths.

MORPHOLOGY. The size, shape, and structure of the organism as it develops in artificial culture vary somewhat in the different media and with age. Some reference to this variability has already been made in connection with the account of the early efforts to obtain pure cultures. Fresh specimens mounted in salt solution, from the culture of glycerin-agar, show a highly refractive organism with a doubly contoured membrane.

The organism is not destroyed by caustic potash. It stains readily with the common aniline solutions, but the stain is rather deep and in many cases too diffuse, and the clearest pictures are obtained by a rather prolonged staining—fifteen to thirty minutes—of carefully made films in a 5 per cent. solution of methylene-blue and then washing well with water. The films are made by suspending a small quantity of the culture in a drop of physiological salt solution or of distilled water and drying. This stain brings out the different parts of the cells, whereas other methods stain diffusely.

Large bodies, such as seen in the tissues of the hand as well as in those of infected animals, are not constant in the cultures. However, as the organism begins to grow on most of the common solid media and under favorable circumstances, it generally presents an outer well-defined but thin membrane, which is separated from the protoplasm proper by a clear and transparent zone. The size varies between 7 and 12 mikrons. The form is round or oval, sometimes polygonal on account of mutual pressure. Budding forms are very frequent, and occur in all stages. The process of budding seems to begin with the appearance of a small projection of the endosporium, which pushes the transparent zone and outer membrane in front of it; very soon these layers enclose the new bud fully, and the point of attachment to the mother-cell may be either flattened or, later, drawn out into a slender pedicle. When the buds are small it is not always possible to recognize the various parts mentioned. In the fairly well-developed bodies the endosporium is vacuolated, and, generally, finely granular. Not rarely some of the granules may be coarse, of varying size, and deeply stained, sometimes producing appearances that resemble the presence of a nucleus, but this is not constant. The vacuole, which may be large or small, is, as a rule, centrally located. Sometimes there is no vacuole. This is generally the case in young, small buds and newly separated bodies. As the culture becomes older the number of really large bodies with large vacuoles seems to gradually increase. The protoplasmic granules, which also become larger, are then either crowded to one side or arranged as a rim around the vacuole. In many of these bodies the transparent zone is no longer distinctly recognizable. Such large bodies are surrounded by numerous much smaller ones, sometimes vacuolated, sometimes not. In some preparations these bodies seem to lie in a gelatinous material.

In a glycerin-agar culture five weeks old or more large bodies are usually quite numerous. In some cultures the size of the cells, the extent of vacuolation, etc., are quite uniform, in others rather variable. The uniform size, regular and characteristic form and large vacuoles of the cells in cultures obtained from an extensive and richly cellular exudate, produced by inserting a quantity of yeast-cells into the anterior chamber of a rabbit's eye, have persisted unchanged through many generations grown on glycerin-agar.

Large bodies with huge vacuoles are also prone to form in cultures on Loeffler's blood serum (Figs. 5, 6, and 7, Plate II.).

With Gram's stain some organisms remain deeply and diffusely stained, while others are partially decolorized, frequently showing, however, three or more deeply colored granules at or upon the margins of the bodies.

By means of stained microscopic sections of the stab cultures in glucose-agar and gelatin it is readily determined that the peculiar lateral outgrowths and branchings observed in these cultures do not depend upon the formation of mycelium, but are composed of budding round forms only. This peculiar way of growing is therefore identical with the development of the curious club-shaped colonies in the gelatin hanging drop.

In liquid media, especially bouillon and Pasteur's fluid, as well as, but to a much less extent, on potato and other solid substance, the organism may be comparatively small. It appears that the buds become separated while still minute. Not rarely a parent cell is found surrounded by a number of minute, free as well as attached buds, many of which are so small as to resemble cocci. Now, these small bodies, which as a rule stain diffusely and homogeneously, may give rise to succeeding generations of small organisms, varying in size from 1 to 5 mikrons. Repeated budding without complete separation may give rise to chains and groups of various lengths and sizes. Certain parts of smear preparations from cultures in Pasteur's fluid and bouillon may resemble very much those of a medium-sized micrococcus, except that the yeast fungus may present rather pronounced variations in size (Fig. 8, Plate II.). When the minute forms cluster closely around large, vacuolated bodies, the first impression, that it concerns a mixed culture, is certainly not surprising.

In some cultures a distinct mycelium develops. This is most notice-

able in Pasteur's fluid and bouillon, but myceliod growth forms may occur to a very slight degree in all media—*e. g.*, plain agar. The formation of mycelium is due apparently to a gradual elongation of individual organisms of the smaller type, resulting in the early stages in irregularly cylindrical shaped bodies, which later grow out into either curved or fairly straight, rather thick rods of varying lengths, or, more rarely, form long coiled threads. Buds may arise from any part of the mycelium, and they may be sessile or pedunculated. When buds separate from the ends of a rod and grow in length, or when all the members in a chain of organisms begin to elongate, a segmented mycelium is formed. The appearance between the ends of two segments of new buds which also grow out long, or the dislocation of a segment from its position in the mycelium, may give rise to quite typical false ramifications. The cylindrical masses, the rods and threads vary in thickness, the average being about 5 mikrons. For the most part the substance of the mycelium is solid and dense, staining diffusely, but parts occur in which there is a membrane enclosing an empty space containing in places finer or coarser granules (Fig. 9, Plate III.).

Cultures on agar-agar are frequently characterized by the production of a granular, yellowish-brown, at times also reddish, pigment. Here are found medium sized typical bodies, quite a few oblong and elongated, narrow, diffusely stained forms, but no typical mycelium, and also a considerable number of round bodies covered and surrounded by yellow or yellowish-brown pigment granules, which are quite uniform in size (Fig. 10, Plate III.). There is no pigment about the long forms. In the early stages of pigment formation the granules appear in the immediate vicinity of the outer capsule, both within as well as outside it. As the amount of pigment about an organism increases, the endosporium disappears—a fact pointing to a pigmentary degeneration of these bodies. The rather limited growth on plain agar has already been mentioned.

Animal Experiments.

1. A minute fragment of the first bit of skin was inserted into the peritoneal cavity of a guinea-pig, which died a month later, greatly emaciated. There were no changes at the point of inoculation, or

in the peritoneal cavity, cultures from the small amount of clear fluid in which remained sterile. The organs contained in pure form the pseudo-diphtheria bacillus, previously isolated from the hand. The liver was extensively necrotic and cirrhotic, but these changes are attributable to the bacillus solely.

2. A white rat was inoculated subcutaneously with 1.5 c.c. of a bouillon culture. A small local abscess formed. The animal died in ten days. The abscess cavity contained a few c.c. of a whitish-yellow viscid pus, from which the blastomyces grew in pure culture. The internal organs were sterile.

Microscopic examination of the abscess wall shows a thin capsule of young fibrous tissue covered by a quite thick layer of pus cells and nuclear detritus, among which rather small, doubly contoured, circular bodies, resembling blastomycetes, are seen. The liver contains a few minute foci of typical granulation tissue, composed of plasma cells, endothelioid cells, small giant cells, and polymorphonuclear leucocytes; but it is not possible to find any typical organisms in these areas. There are quite a number of small, similar foci in lungs, especially around the bronchi, and in the giant cells of these areas occasional rather typical round bodies are observed. The other organs are normal.

3. A gray mouse died five days after receiving 1 c.c. of a bouillon culture subcutaneously. The abscess which had formed contained the organism in pure culture, while the internal organs were normal.

4. A medium-sized rabbit died forty-eight hours after a subcutaneous inoculation of 2.5 c.c. of a bouillon culture. Cultures from the internal organs remained sterile. There is an extensive coccidiosis of the liver. There were numerous minute foci in the lungs composed of epithelioid and giant cells, as well as leucocytes, with considerable nuclear degeneration. In some of the giant cells are circular bodies resembling the organism injected, as well as small, round bodies that stained rather diffusely with methylene-blue, presenting a faint peripheral transparent zone. (There is no record of the condition at the site of the inoculation.)

5. A white rat received 1.5 c.c. of a bouillon culture. Viscid, yellow pus formed about the point of inoculation, and the organism was reclaimed in pure culture. The animal died five days after the injection. The internal organs contained the staphylococcus albus.

6. A gray mouse was inoculated subcutaneously with 1 c.c. of a bouillon culture. It died in five days. The small abscess that had formed contained the organisms, as well as staphylococcus albus. The latter organism was present in all the internal organs.

7. A small part of a colony on agar was inserted into the anterior chamber of the left eye of a large male rabbit. There gradually developed a hypopyon, with softening and threatened destruction of the cornea. The animal was killed after two weeks. The internal organs macroscopically healthy. The anterior chamber filled to distention with a semi-solid, yellowish-gray material, which, when spread out on cover-slips and treated with hydrate of potassium, contained numerous spherical bodies. Inoculations with this material on glycerin-agar gives a rich and pure growth of the blastomyces. Cultures from other organs sterile. Sections of the eye show the anterior chamber to be filled with cellular detritus, among which are a number of round, deeply stained bodies, surrounded by a rather faint halo but no distinct outer membrane. The lens is largely softened, and the iris is the seat of a diffuse cellular infiltration. The iris also contains rather small, deeply stained, round bodies, which at times are surrounded by minute, hyaline-like formations that take the methylene-blue stain very intensely.

8. A small bit of a yeast culture on glycerin-agar was inserted into the anterior chamber of a large white rabbit. The anterior chamber rapidly filled with a white exudate, the cornea became opaque, and a mucopurulent conjunctivitis developed, which soon ceased. Three weeks after the inoculation the cornea had become quite opaque and vascularized, and the anterior chamber contained a large, roundish yellow mass, which has since slowly enlarged. At present, February 27, 1899, the eye is of about normal size, apparently blind, and the yellow growth does not show any signs of diminution. The rabbit seems to be in good general health.

9. A guinea-pig received 1 c.c. of a bouillon culture in the abdomen. It remained quite well, and was killed five weeks later. There were numerous small, grayish-yellow, translucent areas in the lungs; the other organs were healthy. Cultures from all the internal organs remained sterile. Microscopically the areas in the lungs consisted of foci of granulation tissue without any giant cells, but with extensive nuclear fragmentation. Only a few round bodies are to be found,

after prolonged search in numerous sections, stained with methylene-blue, as well as by other methods.

10. A white rat received 1 c.c. of a bouillon culture in the abdominal cavity. It died thirty-four days later. The lungs contained pinhead sized and larger areas of a grayish, rather soft appearance. Smears from these, treated with caustic potash, showed numerous large, round, doubly contoured bodies. The microscopic sections showed extensive bronchopneumonic areas of an inflammatory tissue, with marked nuclear fragmentation and quite a number of large round bodies, which stained diffusely. (Unfortunately, no cultures were made in this case.)

11. A medium-sized rabbit was injected with 0.5 c.c. of a bouillon suspension through the ear vein. Considerable swelling resulted, which healed after three weeks with marked deformity. The animal, which seemed well, was killed thirty-seven days later. The lungs contained a few small nodules; the liver was the seat of a marked coccidiosis. Cultures from all the organs remained sterile. Sections from the lungs show miliary foci of young granulation tissue, but typical blastomyces are not to be found.

12. A medium-sized dog was injected with 2 c.c. of a bouillon suspension into the peritoneal cavity. The animal remained well, and was killed forty days later. All the organs were normal and sterile.

13. A large black rabbit received into the circulation 4 c.c. of a bouillon suspension of a culture on beer-wort-agar. It died during the following night. The lungs were œdematous, the thymus ecchymotic, the liver swollen, soft, and mottled. The spleen and the kidneys appeared normal.

Bacteriological Examination. Smears from the various organs show numerous clear, round bodies not destroyed by KOH; they are most plentiful in the smears from the lungs and kidneys.

Inoculation from the various organs on glycerin-agar give rise to numerous colonies of blastomyces, most numerous in the tubes from the kidneys. The cultures from the liver and spleen also contain the colon bacillus. Only one colony of budding fungi developed in the tube from the heart's blood.

Histological Examination. The lungs are extremely congested, and the capillaries seem to contain rather many polymorphonuclear

leucocytes. In the alveolar walls are numerous small foci of cell accumulation, with marked nuclear fragmentation, and quite typical blastomycetes are found in the interior of some of these areas of necrosis. The alveoli and bronchi contain a fine, granular material, in which lie occasional round homogeneous bodies.

The liver and spleen show no special changes.

The kidneys show quite extensive changes in the glomeruli, consisting in a granular disintegration of smaller or larger portions of some of the capillary tufts and of a more or less pronounced general accumulation of granular detritus in the subscapular space, the cells in the lining of which are generally well preserved. The epithelium of the convoluted tubules is very granular, and the lumen is filled with granular material. The vessels are generally congested. Lying in the glomeruli, the intertubular vessels, and in the granular material are a few oval or round bodies about as large as a red blood-corpuscle, which stain diffusely with the gentian-violet of Gram's method.

14. On February 15, 1899, a guinea-pig, weighing 392 grammes, received in the abdomen 12 c.c. of a bouillon culture of the blastomyces heated to 59° C. for one hour. It became rapidly emaciated. On February 17th it weighed 340 grammes, on the 20th 285 grammes, on the 22d 250 grammes; it died on the 22d. There was marked emaciation, but no macroscopic lesions in any of the organs or tissues. Cultures from the organs and from the heart's blood remained sterile.

Remarks.

The organism here described differs considerably from the blastomyces dermatitidis of Gilchrist and Stokes, which so far is the only blastomyces of similar origin with which to make comparisons. Hesser's brief description, in his preliminary report on the organism isolated by him from a small cutaneous or subcutaneous abscess, only contained a few general statements. Our organism grows much more rapidly than the one of Gilchrist and Stokes; the formation of mycelium is not nearly so marked as in their cultures, in which were not seen the peculiar down- and out-growths and lateral branchings nor the pigment formation on agar-agar characteristic of the blastomyces now described. Both organisms correspond, however, in their

action on gelatin, which is not liquefied in the non-production of indol, and in the complete absence of fermentation of various sugars. Morphologically they are also quite or nearly alike. Gilchrist and Stokes make no mention of such great variability in the size as observed in our organism.

With regard to the pathogenic action of these two organisms, attention may be called to the great similarity, amounting to perfect identity, in the histological changes produced by them in the human skin. The marked epithelial hyperplasia, the diffuse more or less chronic inflammatory processes associated with the formation of giant cells, and of the characteristic miliary abscesses in the epithelium and elsewhere in the skin, together with the presence, especially in the abscesses, of the round, double contoured, budding organisms, constitute the histological picture of blastomycetic dermatitis as now understood. Gilchrist and Stokes found that the blastomyces isolated by them would produce nodules of a chronic inflammatory nature when inoculated into the dog, horse, sheep, and guinea-pig, whereas white mice and rabbits seemed immune. Our organism may be said to be pathogenic to rabbits, guinea-pigs, white rats, and gray mice. It is probably harmless as to dogs,[1] as far as can be judged from one intraperitoneal inoculation of this animal. Its local action may be characterized as necrotic and leucotactic, associated with or followed by the growth of an inflammatory granulation tissue, corresponding, in the latter respect, to the majority of the pathogenic yeasts studied by various Italian investigators, by Lydia Rabniowitsch and others. Its general action may be regarded as slowly toxic, leading, after a varying length of time, to death from marasmus, and, as experiment No. 14 shows, the dead cultures possess a marked marantic effect. It corresponds, therefore, very closely to those varieties of pathogenic blastomycetes which, according to Casagrandi,[2] produce local necrotic

[1] Since writing the above the following experiment has been made: On March 22d 8 c.cm. of a bouillon suspension of blastomycetes were injected into the jugular vein of a small dog, which died greatly emaciated April 17th, the autopsy and microscopical examination showing minute foci of granulation tissue throughout the lungs, and softened cellular areas with yellowish contents in the medullary portion of the kidneys. The blastomycetes were recovered in pure growth and in large numbers from the lungs and the kidneys. No growths of any kind resulted from the inoculation on glycerin-agar and blood serum of 1 c.cm. of the heart's blood.

[2] Ueber die pathogene Wirkung der Blastomyceten, Centrabl. f. Bakt. Abth. I., 1898, xxiv. p. 754.

or suppurating foci, or permanent nodules and a fatal marasmus. It could, probably, not be said that toxic and marantic effects have been so pronounced as to have been definitely recognized in the few carefully observed instances of human blastomycetic infection so far recorded, but certainly the marked decline in weight noted by Prof. Hyde in this case is very suggestive of this effect, and is, therefore, in full accord with the experimental observations.

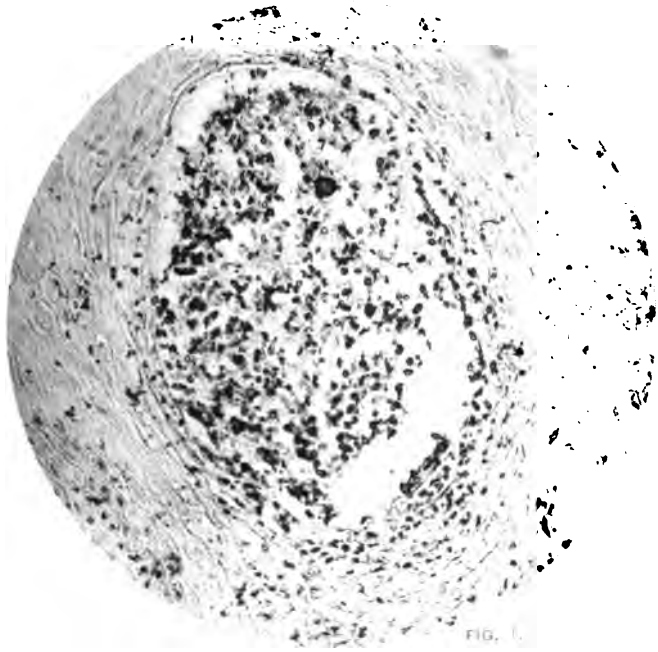
That certain blastomycetes may produce more distinctly suppurative changes in the skin and also elsewhere in man, as well as in animals, has been clearly shown in the now classical case of Busse,[1] by Hessler's case, and in the experimental study of the question of suppuration from yeasts by Nesczadimenko.[2] In connection with this reference may also be made to the instance of refractory subcutaneous abscesses caused by a fungus possibly related to the sporotricha described by Schenck.[3]

To return to the consideration of the blastomycetes studied by Gilchrist and Stokes and by me, it might be regarded as quite clearly demonstrated from the foregoing that the clinical and histological pictures of blastomycetic dermatitis, which from these aspects would appear as a distinct entity, may be produced by organisms which differ so much in certain cultural and pathogenic characteristics that they must be regarded as separate, though closely related, varieties. In view of the present unsatisfactory status of classification of the lower fungi and the blastomycetes, it is desirable to refrain from becoming dogmatic. Casagrandi, for instance, found it quite impossible to classify the blastomycetes upon either morphological or biological grounds, because of the pronounced variability of the individual forms.

[1] The dermatological aspects of Busse's case has been fully considered by Buschke in an article entitled "Ueber Hautblastomykose." (Verh. d. vi. Deutschen Dermatol.-Congresses). Unfortunately this article came to my notice too late to be considered at this time.

[2] Zur Pathogenese der Blastomyceten, I Hefeeiterungsfrage. Centralbl. f. Bakt. Abth. I., 1899, xxv. p. 55.

[3] Bulletin of the Johns Hopkins Hospital, 1898, ix. 286.



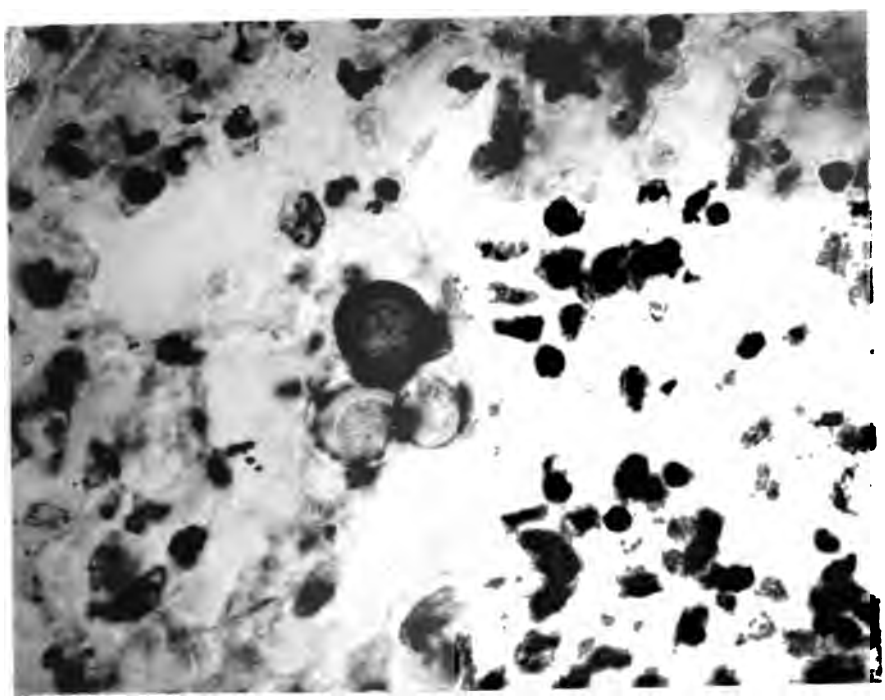


FIG. 2.

HEKTOEN—CASE OF BLASTOMYCETIC DERMATITIS.

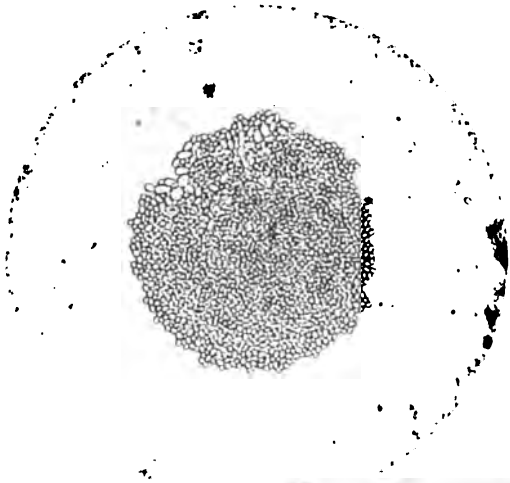


FIG. 3.

FIG. 4.

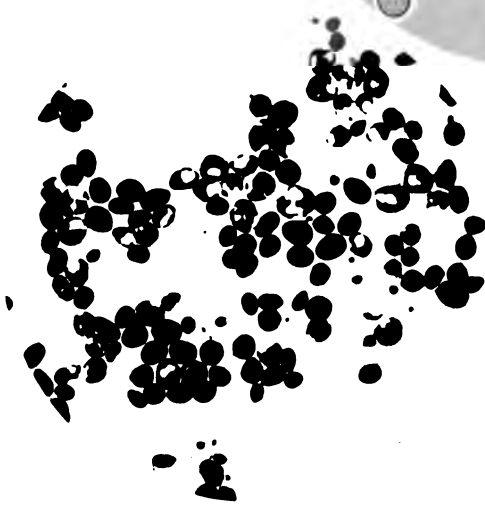


FIG. 5.

HEKTOEN—CASE OF BLASTOMYCETIC DERMATITIS.

FIG. 6.

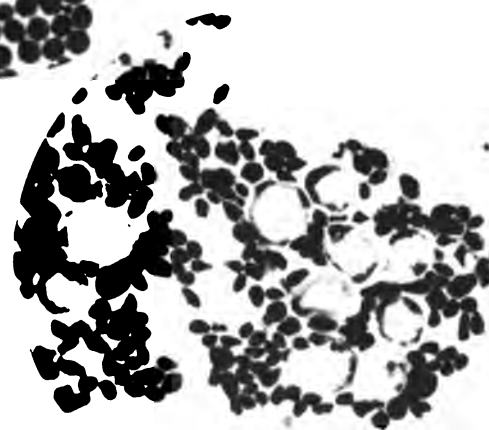


FIG. 7.

FIG. 8.

HEKTOEN—CASE OF BLASTOMYCETIC DERMATITIS.

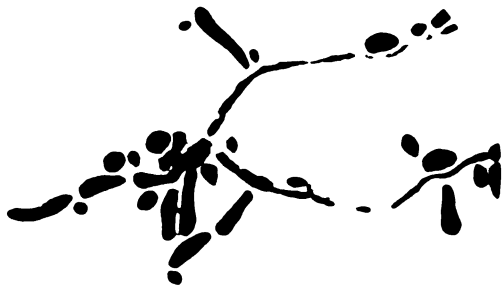


FIG. 9.

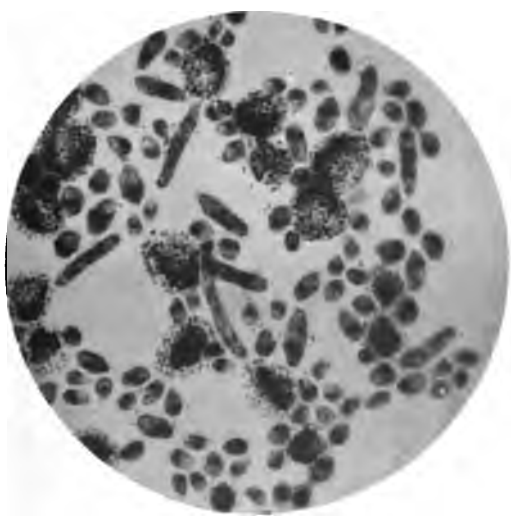


FIG. 10.

HEKTOEN—CASE OF BLASTOMYCETIC DERMATITIS.

Explanation of Plates.

Plate I.

Fig. 1. A miliary abscess in the epithelium of the hand, containing in its upper half a group of three organisms. × 220.

Fig. 2. The three organisms in Fig. 1*a*, more highly magnified. × 1500.

Plate II.

Fig. 3. A colony of the organisms on glycerin-agar. × 250.

Fig. 4. The organism as seen in a hanging drop culture of bouillon. × 1000.

Fig. 5. Vacuolated and solid diffusely stained organisms from glycerin-agar culture. × 1000.

Plate III.

Fig. 6. Budding organisms. Gentian-violet. × 1000.

Fig. 7. Large vacuolated and small solid bodies from a blood serum culture five weeks old. × 1000.

Fig. 8. Chains of the minute form. × 1000.

Plate IV.

Fig. 9. The development of mycelium with sessile and pedunculated buds. × 1000.

Fig. 10. The development of pigment granules around and upon some of the larger cells in cultures on plain agar. Several elongated forms are present. × 1000.

AN EXPERIMENTAL RESEARCH INDICATING THAT PARAXANTHIN-POISONING IS NOT THE CAUSE OF EPILEPSY OR MIGRAINE.

By FRANZ PFAFF, M.D.,
of Boston.

With Introduction.

By JAMES J. PUTNAM, M.D.,
of Boston.

Toxæmic theories, to account for the outbreak of functional nervous disorders, have long exerted a fascination proportionate alike to our sense of the inadequacy of other sorts of explanations and to our growing recognition of the fact that it is to physiological chemistry that we must look for the next great step toward the solution of many of these mysteries. This fact will readily justify renewed discussion of the interesting theory proposed by Dr. Rachford, in 1895, to account for migraine and migrainous epilepsy, and other paroxysmal affections of the nervous system.

Dr. Rachford stated, as will be remembered, that he had found the urines passed immediately after such attacks as these to contain relatively large amounts of paraxanthin, which in normal urine is present only in minute proportions, and that these specimens showed a greatly increased toxicity when injected into mice.

The literature of the subject, so far as these particular observations are concerned, is not large. Dr. Rachford himself has published several papers,[1] and reference has been made to his observations by various writers at home and abroad, but, so far as I know, no control experiments have hitherto been reported.

The matter seemed of such importance that Dr. Pfaff agreed, nearly

[1] See Transactions of the Association of American Physicians, 1895-1897.

two years ago, at my request, to repeat Rachford's experiments, using specimens furnished by my private and hospital patients.

The analyses proved to be tedious and troublesome, usually requiring, as Dr. Pfaff will state, three months or more for completion, and it is partly owing to this fact and partly to the difficulty of obtaining suitable cases, especially of typical migraine, that we can offer but a small aggregate number of observations. Nevertheless, it is justifiable to base conclusions upon them, because the results obtained were satisfactory in the sense of being uniform.

Fourteen specimens of urine, of not less than four litres each, from four of migraine and ten of epilepsy,[1] have been analysed, each specimen representing the quantity passed during and immediately after an attack, the latter being collected until it made up the four litres. The epileptic patients were of different ages—young, middle-aged, and elderly—and the case of one of the latter was of the sort that Rachford specifically refers to as important—that, namely, where epilepsy supervenes on typical migraine.

For the sake of comparison and in order to collect paraxanthin, five thousand litres of essentially normal urine were obtained by Dr. Pfaff from prisoners in the Suffolk Jail, and a large quantity from patients in the Massachusetts General Hospital.

The experiments did not confirm Dr. Rachford's conclusions as regards paraxanthin, and did suggest another possible cause of the toxic symptoms which he observed in the guinea-pig and mice experiments.

We wish to express our appreciation of Dr. Rachford's courtesy in aiding in the research by sending us one of his final fluids.

Whatever may be the conclusion in regard to the particular point here at issue, the only way in which the truth can be arrived at is by investigating each new lead that suggests itself, and then by comparing our results.

Unfortunately, even when toxic substances are found in the excretions in association with attacks of nervous symptoms, it cannot be confidently asserted that we have to deal with a cause rather than with an effect of the outbreak or of the outbreak's cause. There are many pitfalls to be avoided, as every one must admit who takes the pains to

[1] One of these specimens, fifteen litres in amount, represented the mixed urines from a number of children of the Epileptic Hospital, at Baldwinville.

read the cautious, critical statements of those who participated in the debate at Berlin last summer upon the poisons of intestinal origin, before the Congress for Internal Medicine.

JAMES J. PUTNAM.

The method which we followed[1] for isolation of paraxanthin from urine was exactly the same which Salomon had used, and which Dr. Rachford had also adopted in his experiments.

The main outline of this method is as follows: The earthy phosphates are precipitated from the urine by ammonia. After standing some time (twenty-four hours) the clear urine is separated from the precipitates by decantation. This ammoniacal urine, freed from phosphates, is precipitated by silver nitrate. The resulting silver precipitate of the different xanthin derivatives is washed with water till the wash-water contains only traces of chlorides and is no longer of urine color. These washed silver precipitates are suspended in water, decomposed by sulphuretted hydrogen, and filtered. The filtrate is then concentrated to a smaller bulk. On cooling, a deposit forms of uric acid and other impurities, from which the clear liquid is separated by filtration. The different xanthin bodies—dissolved in this solution—are precipitated now for the second time with silver nitrate, the solution having been previously made alkaline with ammonia. The resulting precipitate is washed, and finally dissolved in hot nitric acid of specific gravity of 1.1. On cooling, a precipitate forms containing the double salt of hypoxanthin, whereas similar salts of paraxanthin and xanthin remain in solution. The latter salts are precipitated in the form of simple silver salts from their solution in nitric acid by ammonia. The resulting precipitate is washed repeatedly with water and again decomposed with H_2S and filtered, and the filtrate evaporated to a small bulk. By a process of fractional concentration the xanthin is separated from the paraxanthin. Both these substances may be so obtained in solid crystalline form.

Dr. Rachford did not isolate the paraxanthin contained in the final solution. He only separated out the xanthin by concentration, and so obtained at last a solution which he supposed to contain paraxanthin, and this solution he called the "final fluid." He claims, however, that urine passed by patients during and after an attack of

[1] This research was made at the laboratories of the Harvard Medical School and the Massachusetts General Hospital.

migraine or migrainous epilepsy or kindred diseases yields a "final fluid" containing paraxanthin in enormously increased quantity (so that a drop of such "final fluid," if injected into mice, may produce poisoning identical with that following an injection of paraxanthin), whereas the "final fluid" obtained from urine passed between the attacks does not contain an increased quantity of paraxanthin. The quantity of urine which is necessary for analysis, according to Dr. Rachford, is usually three litres, though a smaller quantity will sometimes give positive results. Dr. Rachford draws the conclusion from his experiments that migraine and kindred disorders (which he specifies) are caused by paraxanthin poisoning. I may add here that Salomon, to whom we owe most of our knowledge of the presence of paraxanthin in normal urine, claims that from one thousand litres of normal urine one gramme of paraxanthin may be obtained; that is to say, one litre of urine contains about one milligramme of paraxanthin. He advises that for detecting this substance fifty to one hundred litres of urine should be taken, since if small quantities are used it may easily happen that no paraxanthin at all will be found in the final solution. Salomon himself failed occasionally to find paraxanthin in quantities of urine varying from six to ten litres.

As already remarked, Dr. Rachford did not isolate the paraxanthin from his "final fluid," relying mainly on his experiments on animals to detect its presence. He injected small quantities of the "final fluid" into mice or guinea-pigs subcutaneously. In certain cases the "final fluid" produced in the animals experimented upon a very marked increase of the reflex excitability of the central nervous system, and he then concluded that this fluid contained paraxanthin in increased quantity. The animals showed in these cases very soon after the injection convulsive movements, which were followed by clonic contractions of all the skeletal muscles. Dyspnœa and gasping respiration, were also present.

In order to become familiar with the process of isolation of paraxanthin from urine, we extracted this substance from five thousand litres of normal urine, collected from the inmates of different prisons in Boston. We obtained from this large amount of urine paraxanthin in quantities corresponding to the results which Salomon obtained, but we could not find any difference between the quantity found in the normal urine and that in urine collected from the different patients.

In a few instances paraxanthin crystals could be detected with the microscope in the residue of the "final fluid" obtained from the urine of these patients. But that substance was never obtained, even from six litres of such urine, in sufficient quantity to justify the assumption that it could account for such toxic symptoms as had been observed to follow the injection of a few drops of the "final fluid" into mice; and, moreover, no such toxic symptoms occurred, provided the fluid was free from impurities, such as chlorides, nitrates, ammonium compounds, and other inorganic substances.

In the tedious process of the preparation of the so-called "final fluid" from urine such impurities are not easily gotten rid of. But the absence of these impurities—which could interfere with the physiological test upon animals—must be clearly proven before any importance can be attached to physiological experiments done with such an indefinite body as a "final fluid" represents.

It will be remembered that in the preparation of the "final fluid" the different xanthin bodies which are present in the normal urine are repeatedly precipitated from their ammoniacal solution by silver nitrates. The silver precipitate of these xanthin bodies is a very voluminous precipitate and retains ammonia and ammonium salts very tenaciously. To free the silver precipitates from the adherent ammonium compounds, it is often necessary to wash repeatedly with distilled water for three or four weeks continuously; otherwise the "final fluid" may contain ammonium compounds in such quantities as would vitiate the conclusions to be drawn from the experiments upon animals.

With one of our "final fluids," from the urine of an epileptic patient, we obtained symptoms of poisoning in mice which corresponded to those Dr. Rachford had seen in his experiments. But on examining more closely the fluid used in this experiment we discovered the presence of a large quantity of ammonium compounds which had remained in consequence of imperfect washing of the silver precipitates of the different xanthins. As soon as we had eliminated these ammonium compounds the fluid lost its toxic property. The toxic effect of the impure final solution had obviously been due to the ammonia it contained, and not, as we first supposed, to an increase of paraxanthin.

The fact that the contamination with ammonia may in fact have

accounted for Dr. Rachford's result is shown by our observations on the one "final fluid" which Dr. Rachford kindly sent us for examination. This fluid produced the characteristic toxic symptoms which Dr. Rachford had claimed as due to paraxanthin-poisoning, but it contained 17 per cent. of ammonia as impurity. After we purified it, so that it no longer contained ammonia, it had no toxic action on mice. On the other hand, a watery solution of ammonium chloride containing ammonia in such quantities as there was found in Dr. Rachford's "final fluid" produced in mice symptoms identical with those of the fluid itself before elimination of the ammonia.

The difficulty of separating the adherent ammonium compounds from the silver precipitates of xanthin and paraxanthin, and of obtaining an ammonium-free "final fluid" for the experiments on animals, had evidently been encountered by another investigator. We received, namely, a "final fluid" prepared in a hospital in Canada, with the request to test it for the presence of paraxanthin. This fluid gave the action on mice which Dr. Rachford had described, but it contained over 20 per cent. of ammonia as impurity and no paraxanthin.

DISCUSSION.

Dr. B. K. Rachford: As Dr. Pfaff has said, I depended chiefly on the physiological test for the identification of paraxanthin in my final fluids. I did not, however, depend exclusively upon this test. I always subjected my final fluids to the chemical tests for xanthin and paraxanthin which I have described in my previous papers.

The xanthin test was as follows: A drop or two of the suspected liquid and two drops of C. P. nitric acid are evaporated over an alcohol lamp; when xanthin is present a lemon-yellow residue is left. This is not changed by ammonium hydrate, but changes into a purple-red with potassium hydrate.

For paraxanthin I used the following chemical tests: A few drops of a concentrated solution of potassium, or sodium hydrate, are added to a few drops of the suspected liquid; a white, glittering precipitate is formed if the suspected solution contained very much paraxanthin; if a little paraxanthin is present the solution will be only cloudy, but will increase in cloudiness after standing a while.

When by these chemical tests I detected the presence of xanthin and paraxanthin in my final fluids, I then made the final test by injecting a drop or two of these fluids into the mouse, or four or five drops into a guinea-pig.

If these animals passed into a tetanus and a little later died in a clonic tetanic convulsion, I then concluded that my final fluids contained an excess of the xanthin group, and expressed the opinion that the important toxic principle in these fluids was paraxanthin. I did not, however, believe that paraxanthin was the only factor in producing these symptoms, and always in my papers spoke of the conditions as a leucomain-poisoning, believing that other leucomains besides paraxanthin were in part responsible for the toxicity of my final fluids. My reason for believing that paraxanthin was the most toxic principle in these final fluids was that the physiological action of paraxanthin as described by Salomon corresponded with the physiological action of my final fluids—that is to say, when the animals were injected the following symptoms resulted: nervousness, extreme reflex excitability, almost a tetanus, and later convulsive movements, clonic tetanic stiffening of all the muscles, dyspnœa, asphyxia, and death in tetanic convulsions.

By these methods I obtained the uniform results which I have described in the papers read before this Society; and here, again, I wish to say that my recent observations have confirmed the opinion previously expressed, that *the xanthin bodies are important etiological factors in producing migraine.*

We are under great obligations to Dr. Pfaff for this valuable contribution, in which he concludes that paraxanthin is not an etiological factor in producing migraine. This work of Dr. Pfaff's was begun and carried on at my urgent request, and the evidence which he has presented is most important in the settlement of this difficult question.

But in the search for truth, it must not be overlooked that I obtained, by the method outlined by me in papers read before this Society, final fluids from the urines of migrainous patients which responded to the chemical tests for xanthin and paraxantnin, and which were toxic for mice and guinea-pigs, with the symptoms above noted; and that I did not obtain from other pathological urines or normal urines final fluids showing the same chemical reaction or having the same toxicity. I made many examinations of urines, and often demonstrated to groups of medical friends the toxicity of the final fluids from migrainous urines, and the non-toxicity of final fluids obtained in exactly the same way from normal urines. These examinations I have made so often, and with such uniform results, that I do not admit that there is room for doubt that the method used and described by me yielded poisonous final fluids from migrainous urines and non-poisonous final fluids from normal urines.

The important question, therefore, is, What are the causes of toxicity in these final fluids? Dr. Pfaff tells us that paraxanthin is not one of them, and that the urines of migrainous patients do not contain paraxanthin in sufficient quantity to make them poisonous. Future observations must determine whether Dr. Pfaff is right in this opinion. But even if Dr. Pfaff be right in his opinion, it does not affect the value of my work in this field. The fact remains that working by approved chemical methods for the isolation of the xanthin bases, I obtained from migrainous urines final fluids which reacted

to approved chemical tests for paraxanthin and xanthin, and which when injected into mice produced the symptoms of paraxanthin-poisoning as outlined by Salomon. It may be that these tests for paraxanthin are not reliable; however this may be, I am quite sure that my final fluids from migrainous urines contained an excess of the xanthin bodies, and that these final fluids were poisonous to mice; and, also, that the final fluids obtained from normal urines did not contain an excess of the xanthin group, and were not poisonous to mice.

Now, a word as to the cause of the toxicity of my final fluids. By correspondence with Dr. Pfaff my attention was called to the possibility that the ammonium in my final fluids might account for their toxicity. By reference to the method which I presented to this Society in 1895, it will be seen that my final fluids would contain a certain amount of ammonium in combination with the xanthin group. After Dr. Pfaff's suggestion as to the toxicity which the ammonium might give to my final fluids, I found that when I eliminated the ammonium from these fluids they lost for the most part their toxicity. This came as a great surprise to me, but still I did not understand why the final fluids from migrainous urines were toxic and those from normal urines were not. Both were treated alike and both contained ammonium in combination. It then occurred to me that my final fluids from migrainous urines, containing more of the xanthin bodies, would for this reason contain more ammonium in combination with this xanthin group. This, however, failed to fully account for the toxicity of my final fluids, since careful chemical analysis showed that as little as 0.1097 per cent. of ammonium in some of my final fluids was sufficient to make them toxic, and that this percentage of ammonium, as found in a solution of any of the ordinary salts of ammonium, was not at all toxic for mice.

The conclusion, therefore, seemed inevitable that the toxic bodies in my final fluids were ammonium compounds of the xanthin bodies, and that these compounds of ammonium were much more poisonous than the ordinary salts of ammonium, such as the chloride.

The suggestion herein contained, that the ammonium compounds with the xanthin bodies play an important rôle in the etiology of migraine is of clinical and pathological importance, and points to the inactivity of the liver as a most important factor in producing this disease. At the present time it seems a well-established physiological fact, that ammonium compounds, especially the carbonate, are the most important antecedents of urea, and that it is an important function of the liver to convert these ammonium compounds into urea. When the liver is extirpated the ammonium compounds in the blood are increased and urea diminished. With these facts in mind one can readily understand how the inactivity of the liver which commonly precedes or accompanies a migrainous attack may result in the accumulation of sufficient ammonium in the blood to combine with the xanthin bodies, which my experiments lead me to believe are in excess in this condition, and in that way contribute an important part to the auto-

intoxication which is the cause of the severe nervous symptoms called migraine.

In conclusion, I may say that at the present time my experiments strongly corroborate this theory, and I need scarcely add that the present mode of treatment of this condition with remedies acting upon the liver and intestinal canal finds support in this theory.

I wish also to say that the final fluid which I sent to Dr. Pfaff contained many times more than the average amount of ammonium found in my final fluids, as I have since learned by careful chemical analyses. Some of them, as I have already noted, contained as little as 0.1 per cent. of ammonium. This is in striking contrast with the 17 per cent. found by Dr. Pfaff in the final fluid which he examined.

DR. HERTER: It is clear from the discussion that has taken place that very opposite opinions are held in regard to the importance of paraxanthin in the production of migraine. It is also apparent, I think, that the ultimate solution of this question, no matter which view is correct, must hang very largely upon technical considerations. It is, therefore, difficult for anybody to express an opinion upon so complicated a problem, unless he has had considerable experience with the very methods spoken of. I have not had sufficient experience to enable me to reach a conclusion on this question, but such as I have had leads me to believe that the burden of proof rests upon Dr. Rachford. I think it is, on the whole, probable that the material that Dr. Rachford has used owes its toxicity not solely to paraxanthin but to substances left in the final fluid, and which it is difficult to get rid of. I have found difficulty in getting rid of both the ammonium salts and the potassium salts of the urine, and either may give rise to symptoms in rabbits that are indistinguishable from the symptoms referred to paraxanthin. I have used the methods employed by Dr. Rachford for the separation of paraxanthin from the urine of migraine, and have obtained entirely negative results, just as Dr. Pfaff has done. I do not feel that this settles the question, but am convinced that the burden of proof rests upon those who contend that migraine depends in any way upon the presence of paraxanthin in the body.

DR. PFAFF: I would like to say a few words in closing. There must be a misunderstanding about the final fluids which Dr. Rachford sent me. (Speaking to Dr. Rachford.) At the time you sent me the fluid you sent a letter saying that it was the fluid from one single patient, and that you had used four-fifths of that fluid and sent me the balance. But I do not think it is necessary to lay much stress upon that.

As to the belief that the final fluid owes its toxicity to the presence of another substance than paraxanthin I think that might be settled in a very simple way. If a final fluid can be prepared from two or three litres of urine collected from such a patient, and if one minim of that fluid would be toxic to

mice, it would correspond to a toxicity about fifty times that of normal urine, and, therefore, a few c.cm. of such urine ought to be a toxic dose for rabbits. Of course, in such experiments, the urine ought to be fresh voided urine, to exclude the error of injecting decomposed urine. Dr. Putnam and I injected into a rabbit intravenously about 80 c.cm. of urine collected from a patient after an attack of epilepsy. The rabbit showed no symptoms of poisoning after the injection of this large quantity of urine. We did not make more experiments in this line, as we did not intend to pursue further this subject.

THE SURGICAL TREATMENT OF TUMORS WITHIN THE SPINAL CANAL.

By JAMES J. PUTNAM, M.D.,

AND

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THE recent studies into the subject of spinal tumors by Bruns, of Tubingen,[1] and by Schlesinger, of Vienna,[2] have been so thorough and so searching, and have so ably carried forward the earlier researches of Horsley, Starr, Sherrington and many others, that it will be long before they are displaced, and seldom that new generalizations of importance will be added to theirs. Schlesinger alone reports fifty-six new cases, and summarizes four hundred, of which one hundred and four come from the post-mortem records of the Vienna General Hospital, which describe a total of thirty-five thousand autopsies. All cases are excluded from Schlesinger's list except where it was expressly stated that the spinal cord was involved, and extradural granulation-growths are not ranked as tumors even when they compressed the cord.

In spite of this array of tumor-cases, the number of actual operations is so small that additional records still have clinical lessons to teach.

The first patient to whose case I shall refer was a lady, aged fifty-two years, whose symptoms, which were very serious, proved to be due to a distinct and easily removable intradural fibroma. The first signs of her illness showed themselves in the early part of 1897, in the form of severe pain, occurring intermittently at first, but in more

[1] Die Geschwülste des N. Systems, 1898.
[2] Beiträge zur klinik des Rückenmarks und Wirbeltumoren, 1898.

and more frequent attacks, over the lower ribs and the left side and down across the abdomen into the left groin. Even a year or two before this she had had an attack of severe pain in the abdomen, for which no cause could be assigned, and which may have been connected with the growth of the spinal tumor, but this had been followed by a prolonged free interval.

In March, 1897, she consulted Dr. R. H. Fitz, whose notes say that the pain was in the region of the transverse colon at first, later in the direction of the descending colon. At that time he saw no reason to ascribe the pain to anything more than neurasthenic and digestive disorders. That summer she went on a driving journey, and this is interesting, because the fact that the jolting of the carriage over country roads did not increase the pain, helped later to the conclusion that the vertebral column had not been primarily involved. It must, however, be admitted that even in cases where jolting does cause pain we should not be justified in concluding that vertebral disease is present, for in the second case which I shall describe, which is one of intramedullary tumor, that sign was present to a striking degree.

In July, 1898—that is, about six months after the first onset of the pain in a definite form—the patient began to notice difficulty in using the left leg, especially where she was obliged to raise the weight of the body on to the step of a carriage or in going up stairs. This is still her greatest difficulty. Slowly but steadily the pain and weakness increased, and it is a noteworthy fact that the former seemed to be closely associated with the condition of the bowels. Not only was the pain made worse by the effort attending an evacuation, which, as has been suggested by Lacquer, may increase the congestion of the intravertebral veins, but the presence of gas in the bowels caused her great distress, and the periods shortly before and shortly after a movement were especially painful times.

Increase of pain in connection with intestinal movements, or constipation, has been repeatedly noted in cases of this sort, but with our patient it was a striking feature. The very presence of the gas which seemed to cause her so much distress was, perhaps, due to a paralytic condition of the bowel-walls. In the report of Ransom and Thompson's case, it is stated that the pain was not worse after breakfast or dinner, but was worse after supper, "when he had some wind."

Slight movements of the head, especially toward the left side, and

even opening the mouth wide would bring on severe pain. It is impossible to believe that the slight contraction of the dorsal muscles required for these movements could, in itself, disturb the inflamed nerve-roots to any considerable degree, but for any one who has studied the neuroses dependent on association, it is quite easy to believe that a faint hint of possible further irritation, such as might attend really extensive movements of the vertebral column, could be given by these slight contractions, and would suffice to precipitate an explosion of pain.

In February, 1898, the patient consulted Dr. R. W. Lovett, literally crawling into his office, in the midst of an excruciating attack of pain which bent her double. From that time even to the present the bent-over position of the body has been assumed as the easiest one, and movements of standing still give rise to more or less discomfort, as they did then to intense pain. All through the spring of 1898 movements of every sort and also the supine position was very painful.

She was first seen by me, in consultation with Dr. Lovett, in the early part of June of the same year. At that time, although she looked in blooming health, she could walk only a few tottering steps, and not those even unassisted. The knee-jerks were greatly exaggerated, the left more so than the right, and ankle-clonus was present. The sensibility to touch and pricking, which had previously been almost normal, was slightly, but only slightly, impaired over the anterior surfaces of the legs and the lower part of the abdomen. At that time the pain, which had been most severe in the neighborhood of the groin, was felt worst over the left flank and lower ribs, especially in the axillary line, where pressure was painful, as is indeed still the case.

The diagnosis of tumor at once suggested itself, as it had already to Dr. Lovett, and the question of operation was canvassed, but as she seemed to improve slightly it was not decided upon until a few weeks later. Dr. Lovett had by that time been obliged to leave Boston for Europe, and left the patient in my charge, with the request to call in Dr. Warren to operate if necessary, and this I shortly afterward decided to do.

Meantime, the impairment of sensibility and motion had increased, until, at the time of the operation, the patient was unable to stand

alone, and had begun to have considerable difficulty in controlling the bladder.

A careful examination as regards the sensibility made three days before the operation showed a very considerable impairment in the entire area of the distribution of the lumbar nerves—that is, over the anterior and lateral surfaces of the thighs, legs, and feet, although not everywhere to quite the same degree. This area of strongly-marked impairment ceased abruptly at the groin on both sides, but slight impairment was observable over the whole abdomen, shading off gradually and finally disappearing at about the epigastric fold. On the whole, the sensibility of the left leg was distinctly better than that of the right, while the loss of motion there was much greater, a fairly certain indication that the left half of the cord had been invaded. Posteriorly, the impairment of sensibility was very much less, both as regards the buttocks and perineum, the back and the thighs. It was, in fact, only on careful tests that any impairment was discovered in these areas. The umbilical reflex was entirely absent for the left side, but was faintly present at the first trial on the right side. In the affected areas the sensitiveness to pricking, temperature, changes of position, and contact were all involved, though not everywhere uniformly.

The character and sequence of symptoms were typical of tumor, consisting first in pain presumably due principally to nerve-root irritation, then signs of cord-pressure, consisting in impairment of sensation on motion, beginning in the toes, and following, to some extent, the "Brown-Séquard" type.

The fact that pain had been felt over the lower ribs, and that the impairment of sensibility was observable as high as the area of the ninth dorsal, coupled with the fact that the patient had never shown any of the other malignant growths nor of vertebral disease, made it reasonable to hope that we had to deal with an extramedullary growth, not primarily involving the vertebral column, and situated as high as the ninth dorsal segment. The high degree of exaggeration of the knee-jerks and the presence of ankle-clonus, taken together with the fact that the sphincters had not been involved early or severely, and that the area of distribution of the sacral nerves was relatively free from signs of impaired sensibility, made it evident that the growth did not seriously involve the lumbar enlargement.

Dr. Warren gives the following account of the operation:

An incision six inches long was made from the seventh dorsal to the first lumbar spines. The muscular mass was rapidly dissected off on each side from the spines and the transverse processes, and held back by a broad retractor devised by Dr. R. B. Greenough. Hemorrhage was controlled by gauze-packing so effectually that it was found at the end of the operation that it had not been necessary to tie a single ligature. The spines of the lower four dorsal vertebræ were next removed with cutting forceps, and the laminæ of the tenth and eleventh vertebræ were cut away, disclosing the dura, but showing nothing abnormal. On removing the laminæ of the ninth dorsal vertebra a swelling was noticed in the cord beneath, which gave to the touch of the finger a marked sense of resistance. On laying open the dura at this point by an incision about one inch in length, a tumor about the size and shape of an olive was disclosed, on the left side, lying in the meshes of the pia. So loose were its adhesions that it was readily removed by the gentlest of movements with a blunt instrument, and with the slightest possible hemorrhage, which was controlled by a gentle pressure of a few moments' duration. No pedicle was found. The dura was stitched with three silk sutures. The muscles were brought into apposition by a few buried silk sutures, leaving a space for temporary gauze drain. The skin was closed with silkworm-gut. Two provisional sutures were left at the point of drainage. A dry dressing was applied.

During the first days after the operation the paralysis of both sensation and motion was intensified, and a zone of hyperæsthesia, such as had not been observed before, covered the abdomen and lower part of the chest, making the reapplication of bandages a very painful process. These results we attributed to the œdema and the disorders of nutrition following the great change in vascular tension. Slight and vague sensations in the legs were felt on the second day, but the first sign of voluntary motion, and that only of the very slightest, was not seen until three days later, and improvement in this respect was extremely slow. The bladder and rectum were not fully under voluntary control for many weeks, and not at all for the first three weeks.

The distress and pain induced by the helplessness, the hyperæsthesia of the abdomen, the constantly recurring cramps of the muscles of the thighs, legs, and feet, made a good deal of the first month a trying period, though it did not pass without frequent indications of

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better things to come. Perhaps even the strange illusions and hallucinations as to the position of the legs and feet, and with regard to movements, with which she was constantly harrassed, were in reality signs of promise.

It is noticeable, that, as in the Gowers and Horsley case, some of the early efforts at voluntary motion excited a spasmodic contraction, or a movement that seemed such to the patient, thought it was in fact a mixture of voluntary motion and spasm.

The first return of perspiration to the legs, which had hitherto been wholly dry, showed itself after several weeks, the moisture being at first confined to the popliteal space, then affecting the surfaces of the legs, which were in contact with each other.

It is always instructive to note how the spinal centres, in spite of long disuse and serious injury, may retain their power of regeneration, but this was still more strikingly shown in the first case by Gowers and Horsley than in ours. This patient, who even before the operation had been paralyzed for months and remained so for a month after the operation, was able at the end of a year to walk three miles.

The case recently published by Eskridge is in almost ever particular a counterpart of the one here reported, but there also the improvement was more rapid.

On the whole, the history of our case since the operation has been one of slow but almost uninterrupted gain. At the present time the patient can walk fairly well with a cane, and short distances alone. Mounting the stairs or stepping into a carriage is very difficult without assistance from behind, but would doubtless be easier were the patient not so very stout. The body was for a long time bent strongly forward during attempts to stand and walk, but in this respect she has improved, though she has not wholly recovered. Every movement is possible and most of them are fairly strong. She still has a good deal of pain from time to time, especially in the back and sides, but I am persuaded that to some extent these pains are due to association and habit, and persist mainly as an echo of the former condition.

A careful examination of the sensibility shows a very slight impairment, in all modes, over the greater part of the legs and abdomen, and even as high as the sixth rib in front; but, as before, there is hardly any impairment in the areas of distribution of the lower sacral

nerves. There is still tenderness on pressure over the lower ribs in the axillary line, but this, too, I am inclined to attribute to the reviving of former associations. There is slight hyperæsthesia over the abdomen, which serves as a reminder of the time after the operation when the arranging of the bandage was a source of great distress. Her greatest discomfort is a sensation of tension in the feet, giving a feeling as if the toes were being drawn upward, and until recently this has been associated with an actual hyperextension of the toes. Indeed, even now an effort of the will is sometimes rêquired to overcome it. The knee-jerks, which remained extremely exaggerated for six months or more after the operation, have now become nearly normal, and ankle-clonus has disappeared. Micturition is normal. The catamenia, which were absent for the two or three months before the operation, have now become normal.

The points in which the case seems especially instructive are the following: The first is the wide extent of area over which pain was at times felt, which embraced the whole zone on the left side, lying between the groin, up to which point the loss of sensibility seemed to be almost complete, to the epigastrium.

One must assume that the pain in the neighborhood of the groin was due not to the irritation of the nerve-root having its main distribution at that level but to that of a nerve-root given off one or two segments higher up, but reaching down to the point in question, for it is impossible to believe that this tumor could have extended down as far as to the origin of the twelfth dorsal root, and all the facts are fairly well accounted for if we accept the views of Sherrington, adopted by Bruns, that every given area on the trunk is supplied with at least three overlapping nerves.

Another point of interest is that the abdominal pain, even from the outset, was increased by the evacuation of the bowels and by distention with gas. I was first inclined, as stated above, to attribute this to increase in the abdominal pressure interfering with the spinal circulation, but it seems to me now more probable that the pain was a referred sensation, occurring on the principles laid down by Head as the outcome of his well-known researches. Most of the cases which Head studied were examples of pain excited by the stimulation of a normal spinal cord through excitations arising from diseased viscera, while in cases like the present we have, perhaps, an example of prac-

tically normal visceral excitations translated into painful cutaneous sensations in consequence of the abnormally sensitive condition of the cord at certain levels.

Another significant fact is that the sensibility in the area of distribution of the sacral nerves was so much less affected than that in the distribution of the lumbar nerves. This seems, to judge by the reports, to be a common occurrence in cases of dorsal tumors. It was noted by Starr in one of his cases, and is especially commented on by Eskridge, who thinks it may be a mark of value in the differential diagnosis of tumor paralysis and Pott's paralysis. For the present I record the fact without offering an explanation, though I think that one is needed.

Finally, I would call attention to the fact that the patient, though greatly improved and able to walk slowly without the aid of a cane, and free from any considerable pain, is yet far from being well. Her present condition still mirrors the distresses both of the time before operation and the convalescence.

The two cases which I have next to report may, I hope, bring encouragement to those who are inclined to operate even where no radical cure is to be expected.

The first case is apparently one of endothelioma of the spinal cord itself, which has been causing symptoms for nineteen years. The patient is a gentleman, now forty-three years of age, who was seized, in 1880, while in robust health, with intense pain in the lumbar region of the back, from which he remained a great sufferer for the next two years. It is noteworthy, in connection with the fact that the tumor probably started from the pia, not from the bone, that the jolting of a carriage greatly increased the pain. At the end of a little more than one year signs of compression or injury of the spinal cord first showed themselves, in the shape of impairment of sensibility to contact and (probably) to changes of position, and slight impairment of motion in the feet, while at the same time the pain diminished and finally disappeared. The spinal cord symptoms continued to progress, until at the end of about nine years he became entirely paralyzed as regards sensation, motion, and control of the bladder and rectum.

In the intervening period the interesting disassociation of the sensory disturbances showed itself, which was for a long time thought to be

characteristic of intramedullary growths or of syringomyelia, but which is now known to be the occasional result of pressure and other lesions. At a time—namely, when he could barely distinguish hot from cold water, and only deep pricks caused pain—he could feel a fly walking upon the skin.

Some years after the paraplegia had become complete the patient's general condition became so poor that chances of relief were eagerly sought. The cause of this state could not be positively ascertained, but he had lost much weight, his face appeared dusky, and he suffered greatly from frequent recurrences of singular attacks of sudden chill followed by fever and sweating, of one, two, or three days' duration, which had occurred at intervals for a number of years, and have, indeed, continued to occur, though much less frequently and with much less severity, up to the present time. It was ascertained by careful investigation that these attacks were not of malarial origin, and the most probable alternative diagnoses seemed to be urethral infection, or some influence starting from the spinal disease.

Although it was recognized as quite possible that the new growth, which was obviously present, lay within the cord itself, still the chance of an extramedullary tumor could not be wholly excluded, as will be readily conceived by any one who has made a careful study of the data on which these diagnoses are based. Therefore, after consultation with Drs. Walton, Keen, and Warren, and by letter with Dr. Mills, of Philadelphia, an operation was decided upon and was performed by Dr. Keen in 1891.

The cord was found enlarged and dark gray or bluish in color, and as no sign of external disease was present, the wound was sewed up. The recovery from the operation was steady, and convalescence was no sooner fairly established than the patient's general health, strength, and flesh began to improve, so that he has been in all respects markedly better ever since. Indeed, at the present time, though the new growth has obviously invaded the cord as high as the lower cervical region, he is in excellent physical condition, and the fever-turns are of rare occurrence.

The favorable state of affairs following the operation was temporarily interrupted in 1895, when he suffered for a number of months with severe grinding pain across the neck and shoulders and in the arms, evidently due to the irritation of the new growth. This was

relieved at first by applications of heat and ice, and he then remained free for more than a year. In December, 1897, however, the same pain returned, with increasing intensity, and continued to grow worse, so that toward the end of January it precluded sleep and became intolerable. After all measures that could be suggested had been tried in vain, I proposed to his physician, Dr. George Washburn, that another operation should be undertaken, at the site of the previous one, with a view of allowing cerebral spinal fluid to drain off for some time, in the hope that changes in circulation and pressure might be induced which would at least break off for a time the habit of pain, for as every one who is familiar with the treatment of neuralgias knows, the effect of habit counts for much in maintaining pain, and, on the other hand, a change of "set" of nervous currents often serves to relieve it. The suggestion was an empirical one, but the result seemed to justify it. The operation was performed by Dr. Warren, who gives the following account: On February 10, 1898, the upper portion of the cicatrix was incised and the arches of the seventh, eighth, and ninth dorsal vertebræ removed. The cord at the seat of the old cicatrix was much thickened, and appeared like a soft sarcomatous tissue. Probing failed to reveal any collection of fluid. A gauze drain was left in and the wound closed. The sinus formed by this drain closed in about two weeks after the discharge of considerable cerebro-spinal fluid. A small bed-sore was easily controlled. An irritable spasmodic stricture caused some trouble at first, on the passage of the catheter, but finally yielded.

The patient never had another untoward symptom, except that for one week after the operation the numbness of the fingers of the left hand, by which he had been occasionally annoyed, increased. This, however, soon diminished, and is now less than before the operation. The pain ceased at once and has never returned.

The spinal cord at the point operated on seemed to have been converted into a dark-colored mass, not suggesting in any respect the normal cord. A piece of it which was excised, and afterward examined microscopically, proved to be made up of a mass of small, round cells, probably endotheliomatous in nature. (Examination by Dr. E. W. Taylor and others.)

The third case is of interest, from the relatively favorable outcome of operation in a case essentially incurable, and also because it is one

where a sarcomatous growth seems distinctly to have been initiated by injury.

The patient, who at the time of my examination was a young man of twenty-four years, had had, three years before, a severe fall from a ladder, in the course of which his neck had received a severe wrench, followed by stiffness and impairment of movement to the left, which was due, as I am inclined to believe, to a partial dislocation. He was able to return to work after six weeks, but in the course of the two following years his neck was injured twice again. Six to eight months before I saw him he began to have difficulty in walking, then in the use of his hands, though, strangely enough, disorders of sensibility, either subjective or objective, have been trifling from first to last. Knee-jerks and wrist-jerks and ankle-clonus soon developed; both legs and arms became wholly paralyzed, with the exception of trifling movements; and gradually the breathing became affected so that eventually it was possible only through the diaphragm and accessory neck muscles.

When matters arrived at this point and death seemed inevitable, he consented to an operation, which I had already advised. I had felt a prominent vertebral body in the pharynx, and believed it probable that he was suffering from caries of the upper cervical vertebræ, with extradural cord compression; but it should be said that my colleague, Dr. G. L. Walton, was less inclined to favor this view than that of sarcoma, which proved to be the correct one.

The operation was done by Dr. J. W. Elliot, who kindly allows me to use his notes, on June 20, 1898. The posterior surface of the axis was found eroded, and on breaking it away with the forceps a sarcomatous mass was found beneath, which apparently penetrated directly to the spinal cord. This was removed and its base curetted, and the surrounding parts, which seemed also to be infiltrated by new growth, were cleared up as far as possible. The growth was pronounced by Dr. W. F. Whitney a giant-cell sarcoma.

The patient's breathing improved at once, and after a few days the voluntary motion began to return to both arms and legs. He left the hospital in three weeks, much relieved, though still unable to walk alone. This improvement was soon followed by a relapse to a certain degree, but this again by renewed improvement some weeks later. Since then he has been gaining steadily and is still gaining. An

examination made within a month finds him in good flesh and color, breathing without effort, free from pain. He has no subjective impairment of sensibility of consequence, and a careful examination shows that the sense of contact, temperature, pain, and position is almost but not quite normal below the neck. The breathing is still mainly diaphragmatic, but the costal muscles also act.

Almost all motions of both arms and legs are possible, and though weakness and rigidity and spasm still incapacitate him from getting about alone, he is able to do many things for himself, and looks forward, with apparent justice, to further improvement.

The number of operated cases already published has increased from the twenty reported by Bruns, in 1898, to thirty-three, which have been collected for us by Dr. Robert B. Greenough, who assisted Dr. Warren at both of his operations, and to whom I take this occasion to express my appreciative thanks. This list does not embrace the five cases of pressure paralysis following Pott's disease, which were included by Starr in his table, nor Starr's own case of extradural tubercular tumor. It is true that these cases differ from the great majority of the Pott paralyses cases, in that the pressure was exerted by thick masses of organized tissue forming tumors on the dorsal surface of the dura, but, nevertheless, it seemed to me that a consideration of them would open the large subject of Pott's disease, upon which I could not enter.

Spinal Tumors Operated on.

No.	Reporter.	Reference.	Date.	Tumor.	Height.	Situation.	Result.
1	Bruns and Kredel.	Arch. Psychiatrie, Bd. xxviii.	1892	Sarcoma.	9 D to lower lumbar	Intra-dural.	Death.
2	Bruns and Lindemann.	Neurol. Centralbl., 1894, p. 359.	1894	Sarcoma.	3 to 6 D	Extra-dural.	Death in 1 day.
3	Curch and Eisendrath.	Amer. Journ. Med. Sci., 1892, p. 395.	1890	Spindle-cell sarcoma.	4 to 5 D	Intra-medull.	Death in 4 days.
4	Clark.	Brain, 1895.	.....	Endotheli-oma.	Lower C	Extra-dural.	Death from hemorrh'ge
5	Curtis.	New York Record, March 5, 1898.	1898	Cancer.	6 D	Extra-dural.	Death in 16 days.
6	Davies-Colley.	Clin. Soc. London, 1892, p. 163.	1892	"Fusiform" spindle-cell sarcoma.	5 to 6 D	Extra-dural.	Recovery.
7	Eskridge and Rogers.	Phila Med. Journ., Feb. 19, 1898.	.....	Tumor of vertebræ.	4 to 5 D	Extra-dural	Death in 9 days.
8	Eskridge and Freeman.	Phila Med. Journ., Dec. 10, 1898.	1897	Fibroma.	3 to 4	Intra-dural.	Recovery.
9	Gerster.	N. Y. Med. Journ., 1892.	.....	Sarcoma.	5 D	Intra & extra-dural.	Improvement.
10	Gowers and Horsley.	Med. Chir. Trans., 1888, p. 407.	1887	Fibro-myx-oma.	3 to 4 D	.....	Recovery.
11	Horsley.	Brit. Med. Journ., 1890, part II.	.....	?	.....	Intra-dural.	Death in 1 day.
12	Horsley.	Clin. Journ., Lond., 1896-97, ix. p. 177.	.....	Echinococ-cus.	(3L n'rve) 12 D V	Extra-dural.	Recovery?
13	Ignatoff.	Vayenno Med. Journ., St. Petersburg, 1896, I sect. clxxxvii. pp. 30-32.	1894	Chondro-sarcoma.	5 to 7 D	Extra-dural	Improvement.
14	Kümmell.	Arch. klin. Chir., 1895, Bd. l.	1893	Sarcoma.	3 to 4 D	.....	Improvement.
15	Lichtheim and Mikulicz.	Deut. med Woch., 1891, p. 1386.	1890	Psammoma.	9 D	Intra-dural.	Death in 2 days.
16	Lichtheim and Mikulicz.	Deut. med. Woch., 1891, p. 1386.	1890	Psammoma.	4 D	Intra-dural.	Marked improvement.
17	Lloyd.	Amer. Med. Surg Bull., New York, 1896, x. p. 659.	1896	Echinococ-cus.	8 D to 5 L	Extra-dural.	Recovery.
18	Laqueur and Rehu.	Neurol. Centralbl., 1891, p. 193.	.....	Lymphan-gioma.	Sacrum	Extra-dural.	Marked improvement.
19	Munroe.	To be published later.	.....	Sarcoma.	Lumbar	.....	Death.
20	Pescarolo.	La Riforma Med., 1892, X. Internal. Cong., Berlin, iv. p. 59.	.....	.....	2 to 5 D		
21	Putnam and Elliot.	.....	1899	Sarcoma.	2 and 3 D	Cerv. vert.	Improvement.
22	Putnam and Warren.	.....	1899	Fibroma.	9 D	Intra-dural.	Great improvement.
23	Quensel and Garten	Neurol. Centralbl., 1898, xvii. p. 482.	1896	Sarcoma.	7 to 8 D	Extra-dural.	Death in 6 days.
24	Ransom and Anderson.	Brit. Med. Journ., 1891, ii. p. 1144.	.....	Echinococ-cus.	10 D	Extra-dural.	Death in 8 days.
25	Ransom and Thompson.	Brit. Med. Journ., 1894, i. p. 395.	.....	Round-celled sarcoma.	8 D	Extra-dural.	Death in 6 days.
26	Roy.	N. Y. Med. Rec., 1890, ii. p. 564.	1890	?	9 to 12 D	Intra-dural.	Recovery.
27	Sänger and Krause.	Munch. m. Woch., 1894, p. 22.	1894	Sarcoma.	6 D	Extra-dural?	Death in 4 days.
28	Sonnenburg.	Verh. Deut. Gesall. Chir., 18th Cong., Berlin, 1889.	.....	Sarcoma.	Lower D	Extra-dural.	Death in 6 weeks.
29	Starr and Abbe.	N. Y. Med. Rec., 1890, p. 85	.....	Sarcoma.	8 to 9 D	Extra-dural.	Death in 9 days.
30	Starr and McCosh.	Amer. Journ. Med. Sci., June, 1895.	.....	Sarcoma.	5 D (7 D)	Extra-dural.	Death in 21 days.
31	Starr and McCosh.	" " "	.....	Lipomata.	Lumbar	Extra-dural.	Imprvem't; death in 6 mos from upper dorsal caries.
32	Szekeres.	Pester Med. Chir. Presse, 1894, p. 43.	.....	Echinococ-cus.	.....	Extra-dural.	Recovery.
33	Welms and Trendelen-burg.	Beitr. z. klin. Chir., 1898, xxi. p. 151.	1896	Echinococ-cus.	2 L to sacrum	Extra-dural.	Death in 6 mos. from amyloid.

Of the thirty-three operations reported in this table, seven led to recovery and ten to more or less improvement, although only in five of these latter, amongst which our first case was included, was the improvement considerable or lasting.

Among the cases reported as "recovered" there are two where the records are not sufficiently perfect to allow of verification of the statement. In one other case (Davies-Colley) the tumor removed was a sarcoma, so that although the patient was able to return to work the eventual outcome is perhaps uncertain.

In ten, perhaps twelve cases, operation seems to have hastened death, which occurred five times through meningitis, septicæmia, or hemorrhage (once in a case of endothelioma); five times through shock, exhaustion, or other causes. It is fair to believe that with improved methods of operation and diagnosis the danger from some of these agencies would diminish, but at the worst the figures show only one out of three chances for hastened death against even chances for some improvement.

In nine cases the operation seems to have made little difference in the progress of the case, and it should be remembered that even with the others the death which was hastened was bound to occur soon at any rate.

The really satisfactory cases for permanent or complete recovery or substantial improvement are few in number. The best results are in the three fibroma cases, one each of psammoma, lipoma, and sarcoma, and two of echinococcus. The occurrence of the last two fibroma cases (Eskridge's and Freeman's and ours), so near together, might suggest that they are of frequent occurrence, but in fact they are separated by twelve years from that of Gowers and Horsley, which was the first successful case ever reported, and which did so much to stimulate the surgeon's hope.

It is interesting to note that in spite of the difficulty—or impossibility in some cases—of deciding positively as to the exact position of a tumor, or even whether it is inside or outside the cord itself, no case *has been reported* where an operation was done on a wholly mistaken diagnosis. In one case, however, the tumor was missed because it lay above the incision, and in another, contributed by Bruns himself, a growth which was supposed to be extramedullary proved eventually to be a diffuse sarcomatous infiltration of the roots and outer portions of the cord.

A few cases—not operative—are on record where the diagnosis, though carefully made, proved wholly erroneous.

How large is the surgeon's field for operation in the spinal canal? This is a question which the physician has to consider, in view of the great uncertainty which must attend his diagnosis as regards the exact position of the tumor, namely, whether it lies dorsally or ventrally with relation to the cord. The possibility of drawing the cord aside to a certain extent, cutting one or two dorsal nerve roots, if necessary, to accomplish it, has been contemplated by various surgeons. In fact, Kümmell[1] removed a laterally placed sarcoma of the body of a vertebra and scraped out the cavity, but no tumor has, to my knowledge, been removed from the ventral portion of a vertebral body.

It is an important inquiry how nearly, in the cases which are counted as successful, such as the first of those reported by us to-day, the improvement is likely to approach absolute recovery, to what extent the degree of probable improvement may be foretold, and what signs make its occurrence improbable.

Very few cases are actually at our command—if we omit those of Pott's disease—for answering this question. In most of the cases that ended in recovery the paraplegia had been complete but for a very brief period, but in the Gowers and Horsley case it had existed for several months. In Pescarolo's[2] case, where the patient had been paralyzed for some years, there was no improvement at the end of five months after operation. No one need be disappointed at the occurrence of a temporary increase of paralysis after operation, or at a delay in the onset of signs of improvement. Some return of sensibility is likely to show itself by the end of a day or two at the latest, but voluntary motion may fail to return for one or two weeks. The earlier movements, as in the Gowers and Horsley case and in ours, although initiated by voluntary effort, may seem to the patient, and at first to the physician, to have all the character of involuntary spasm.

It is probable that, as a rule, the prospect is better in the cases where the paralysis develops slowly, as from the gradual increasing pressure of the large flat masses of inflammatory exudation met with in Pott's disease, than where it comes on rapidly, since in the latter case the nerve elements and bloodvessels do not have the same opportunity to accommodate themselves to the lessening space. In cases

[1] Arch. für Chirurgie, 1895.

[2] Citation by Bruns.

of the former sort, a delay of a few weeks, or even days, in operating may be of far more consequence than that of an equal number of months under other circumstances.

Schlesinger points out, and his opinion is corroborated by that of others, that the cause of the paralysis is complex, and that it includes the effects of pressure, anæmia, necrosis, œdema, and also of inflammation. The latter element is of special importance, because, in the opinion of Horsley[1] and others, it is liable to increase after operation —though, on the other hand, Allingham offers evidence that it may occasionally diminish. Indications that the cord is not only compressed but softened are, however, in Bruns' opinion not a positive contraindication to operation.

To what extent is it worth while to operate where there is little prospect of inducing a cure? This is a question which each physician and surgeon must answer for himself, and with reference to the individual circumstances of each case. I do not, myself, believe that the surgeon should throw the decision too much upon the patient. The alternatives which he is bound to offer (let him express them as simply as he may) are bound to be bewildering, and the choice which the patient makes is far less likely to be a good one than that which the conscientious physician can make for him.

Bruns believes that when the diagnosis of tumor is fairly made it is usually best to operate, but that this diagnosis can rarely be conclusive until signs of actual cord pressure have appeared, and even then the outcome is largely a lottery.

The second and third cases reported by us give some ground for greater hopefulness in prognosis than an interpretation of reported facts in the light of our narrow knowledge might seem to justify. Sometimes the operation appears, in accordance with some subtle principle, to induce to a new "set" to the tendencies at work. The tumor may, perhaps, be led to grow in a new direction; or, as in the second case reported by us, the temporary relief to pain may introduce a fairly persistent relief. The history of neuralgias of other sorts gives abundant illustrations of this sequence. Thus the biographer of Lord Lawrence tells how, while he was Governor of the Northwestern Provinces of India, and had been for a long time a sufferer from facial neuralgia—usually so intractable—the news was brought of the out-

[1] British Medical Journal, 1890.

peripheral nerves nor of the spinal nerve roots, and believes that they represent spinal segments of the gray matter. The boundaries of his areas do not run parallel with the ribs, but are at right angles with the long axis of the body, thus corresponding with a type of arrangement which has been repeatedly noted in descriptions of sensory disorders resulting from spinal tumors. He also calls attention to the fact that the increased sensitiveness of the skin, associated with visceral irritation, is not a real increase of the contact sense, but is to be classed as a painful affection—*i. e.*, as a hyperalgesia and not a true hyperæsthesia. This is also true of the area of sensitiveness which lies just above that of anæsthesia in tumor cases.

It can hardly be doubted that some of the curious relationships between certain conditions of the visceral organs and the pain in spinal tumor are best explained by the aid of Head's observations. Thus, in our first case, one of the most serious causes of exacerbations of pain was the slight distention of the bowels with gas, and the conditions present immediately before and after a movement. One might possibly adopt the explanation suggested by Lacqueur for the pain attendant on straining at stool—namely, the disturbance in the abdominal and secondarily spinal circulation—but it is at least an equally reasonable hypothesis that the effect was due to the slight but additional irritation of the affected segments of the spinal cord. Even though the pain was not strictly confined to the cutaneous areas most closely related to some particular viscus, but represented only an increase of the habitual pain due to the tumor, the same explanation will hold good, for Head's observations show that these sensory reflexes follow a similar law to that which governs motor reflexes, in that two factors are at work. As soon as any stimulus reaches the gray matter of the spinal cord it instantly diffuses itself, and although the effect most likely to follow will tend to confine itself to the level at which the nerve conveying the stimulus first terminates, yet if a peculiarly irritable condition of the gray matter exists at another level the response may come from that, and the next time the same result may occur more readily through the action of the law of association and habit. It is in the same way, I think, that the effect of gaping and sneezing, and even, as in our case, slight movements of the head and face, come to exert such a strong influence in exciting pain. It is doubtless true that these movements produce slight changes of tension within the spinal canal, but these must be so slight that they would

fail to be effective for harm had they not been at the same time associated with stronger movements, which were capable of drawing, to a material degree, on the inflamed parts.

The consideration of our first case calls to mind another point of both theoretical and practical interest. It was, namely, very noticeable that the area supplied by the lower sacral nerves—that is, the well-known saddle-back area—retained its sensibility to a far greater degree than that supplied by the lumbar portion of the cord, although that was wholly below the point of pressure. This condition of affairs is found repeatedly in many of the observations, and Eskridge calls attention to this as perhaps characteristic of tumor cases. One may offer theoretical explanations based on mechanical principles, but the fact is worthy of being placed side by side with the observations (not invariably correct [Lacqueur]), that when the cauda equina, as a whole, is injured, it is pre-eminently these same lower sacral nerves, though they occupy a protected position in the middle of the aggregate bundle, which are most affected, and also with the fact pointed out by Bruns, that the root symptoms provoked by intradural but extramedullary tumors are usually referable not to pressure upon the nerve roots in their course but to pressure exerted at their point of exit from the cord.

With regard to the favorable results which followed operation in the second and third cases reported by us, it would be hazardous to assert that they are so clearly attributable to the operation as to repetition of the procedure in similar cases. This is not the first time where the spinal canal has been opened in cases of intramedullary tumors, though sometimes the condition actually found was a surprise. This happened in the case reported with such care by Bruns, and there also, as a matter of fact, a considerable degree of improvement as regards pain, followed the operation.

The consideration of the lesions met with in these compression cases, as shown by the history of Pott's myelitis and of the tumor cases reported by Bruns, Schlesinger and others, suggests reasons enough why the improvement in some of these cases is so much greater than it is in others. For some reason not clearly definable the effects of compression sometimes lead to hemorrhages and necrotic softening, both at the point of the greatest narrowing and occasionally a little higher than this as well, while at other times such lesions are wholly absent, although the stricture may reach a high point.

A CASE OF HÆMOCHROMATOSIS.

THE RELATION OF HÆMOCHROMATOSIS TO BRONZED DIABETES.*

BY EUGENE L. OPIE, M.D.

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WIDELY disseminated pigmentation of the organs of the body is a conspicuous phenomenon, and at autopsy cannot readily be overlooked. The physiology of pigmentation is but little understood. Pathological pigmentation is involved in even greater obscurity. For this reason the following case has been considered worthy of study. It represents, I believe, an intermediate stage between two conditions which, though rare, have elicited much discussion—namely, hæmochromatosis of von Recklinghausen and the bronzed diabetes of Hanot and other French writers. The case to be described occurred in the practice of Dr. Thomas Opie.

CASE.—Male, white, aged fifty-five years. The history which it has been possible to obtain is meagre. The individual, though never very robust, had enjoyed fairly good health. There was no history of alcoholic excess. He was married and had several children. His wife was healthy. For several months he had resided in Puerto Rico, and until six or seven weeks before his death was able to continue his work of surveying. The onset of his final illness occurred with symptoms indicative of typhoid fever. When first seen, two weeks later, he was evidently very ill. There was elevation of temperature, and rose-spots were present upon the abdomen. Deep pigmentation of the skin attracted immediate attention, marked universal bronzing suggesting Addison's disease. Jaundice was not present. The urine at no time during the period of observation contained sugar. The first examination was made four weeks before death. Three days before death the urine was clear, of deep amber color, and contained neither sugar nor albumin.

* This paper was presented to the Association in behalf of Dr. Opie by Dr. William H. Welch.

The reactions of bile pigments were not obtained. The blood-serum caused the agglutination of the typhoid bacillus. Death occurred with increasing weakness.

Autopsy. Performed nine hours after death. The body, 170 cm. in length, is that of a very thin, sparely built man. The skin over the entire body shows deep pigmentation of a bronzed metallic hue, most marked upon the back of the hands, about the nipples, and upon the penis, where, just above the corona, the skin has a deep brown color. The conjunctivæ are clear; the abdominal wall contains a small amount of deep yellow fat.

Peritoneal Cavity. The parietal peritoneum, as well as that of the intestines, shows a varying degree of bluish discoloration. The appendix is fixed behind the cæcum by fibrous adhesions; the enlarged spleen is adherent to the diaphragm.

Thorax. The lungs are free from adhesions and the pleural and pericardial cavities contain no excess of fluid.

Heart. Weight, 280 grammes. The muscle, of a yellowish-brown color, is soft and flabby in texture. The intima of the coronary arteries is roughened by a few yellow, raised patches.

Lungs. The left lung is everywhere crepitant. Upon the surface of the upper lobe of the right lung are seen several prominent areas, about 2 cm. across, over which the pleura is dulled. The tissue below is firmly consolidated, and on section has a grayish-red, finely granular surface. Several larger areas of similar consolidation are present in the lower lobe. The bronchi are intensely injected.

Liver. Weight, 2270 grammes. The surface is of a deep reddish-brown color of peculiar character, resembling that of iron rust. The surface of the left lobe, more markedly than that of the right, is superficially nodular and puckered, presenting in a moderate degree the appearance of a hobnail liver. On section islands of lighter brown parenchyma, representing one or several lobules, are surrounded by fibrous stroma of a deeper brown color. Sparsely scattered are opaque yellowish-white areas, often 1.5 mm. across. The gall-bladder, distended by thin green bile, measures 12 cm. in length.

Spleen. Weight, 700 grammes. The organ is soft and on section the almost diffluent pulp has a deep red color. The Malpighian bodies are prominent.

Stomach. The mucous membrane shows everywhere a deep greenish-black discoloration, evidently not due to post-mortem change. Along the lesser curvature there are a few areas of relatively normal yellowish-white appearance, but elsewhere the pigmentation is uniform.

Intestine. The duodenum has a greenish-black discoloration almost equal in intensity to that of the stomach. This pigmentation is not uniform, and upon the areas of lightest color are seen deeply pigmented, slightly raised nodules about 1 mm. in diameter. The jejunum is less markedly pigmented than the duodenum, while the ileum is of even lighter color, though still preserving a greenish-gray tint. Throughout the lower portion of the ileum, for the most part upon the Peyer patches, are small round or slightly irregular ulcers, with sharp edges and clean base, in which are occasionally seen

exposed fibres of the circular muscular coat. Ulceration is most extensive immediately above the ileo-cæcal valve. The colon exhibits moderate greenish-gray discoloration. The distal 1.5 cm. of the appendix is obliterated.

Pancreas. Weight, 170 grammes. The organ is of large size, measuring 16 cm. in length, and is very firm in consistence. On section the cut surface has a uniform deep chocolate-brown color. The capsule contains much fat, and extending inward from it are septa of adipose and fibrous tissue.

Adrenals. Combined weight, 10 grammes. No abnormality is observable.

Kidneys. Combined weight, 470 grammes. The capsule on removal leaves a smooth surface. The cortex, of an average thickness of 7 mm., has a red cloudy appearance.

Bladder. Mucous membrane is normal.

Testicles. The cut surface has a light brown tint. The prostate and seminal vesicles are normal.

Lymphatic Glands. In the retroperitoneal tissue near the hepatic vein, behind the stomach, above and below the pancreas, and on either side of the aorta as low down as its bifurcation, are enlarged, moderately firm lymphatic glands. On section they have a uniform, brilliant orange-yellow surface. In the gastrohepatic omentum are enlarged glands of a similar nature.

Cultures. From the heart's blood the typhoid bacillus was obtained in pure culture. The same organism was obtained from the liver, gall-bladder, and kidney. The bacillus lactis aërogenes was found in the lung and kidney. The colon bacillus was grown from the pancreas. A culture from the spleen remained sterile.

Anatomical Diagnosis. Typhoid fever, ulcers in the ileum, acute splenic tumor, cloudy degeneration of the kidneys, bronchopneumonia. Hæmochromatosis: pigmentation of the liver, pancreas, heart, stomach, intestine, peritoneum, lymphatic glands, skin, and testicles. Cirrhosis of the liver. Chronic interstitial pancreatitis.

HISTOLOGICAL EXAMINATION. The organs which show the most marked pigmentation are the liver, pancreas, heart, and gastro-intestinal canal.

Liver. Advanced cirrhosis is indicated by the presence of wide bands of fibrous tissue, occupying one-half to one-third of the area of the cut surface and separating the parenchyma into islands which represent one or several liver lobules. These septa, which are densely fibrous and, in general, poor in cells, surround both the portal spaces and sublobular veins. There is but little invasion of the periphery of the lobule by fibrous strands, but surrounding the central vein a mass of tissue penetrates the lobule and sends out irregular, radiating projections along the capillaries between the columns of liver cells. The most conspicuous feature of the histological picture is the immense amount of brownish-yellow pigment present, both in the parenchyma and in the interstitial tissue. In the liver cells the pigment is found in varying quantities. When in moderate amount it is situated in that part of the cell most distant from the capillaries, consequently occupying the central part of the columns of liver cells. The pigment is deposited in the

form of brilliant, brownish-yellow, relatively coarse granules, round or polygonal in outline, and of slightly variable size. The endothelial cells of the capillaries and Küpffer's cells contain granules of similar character. The accumulation of pigment in the newly formed fibrous tissue is even greater than that within the parenchyma. Here it exists in part as fine granules within spindle-shaped cells, of which some are apparently fibrous tissue cells, while others represent the endothelial lining of capillaries or lymphatics. The greater quantity of the pigment is, however, not contained in cells. While this extracellular pigment is of the same yellowish-brown color as that abundant in the cell, the individual particles vary greatly in size, globules being often found whose diameter is two or three times that of a red corpuscle. These pigment particles are, as a rule, collected into small clumps, and between the clumps are at times small round cells.

The hepatic cells which contain a moderate amount of pigment are, in general, normal in appearance. In specimens stained with methylene-blue the cell protoplasm is found to contain in great abundance granules of varying size and shape, taking a deep blue stain. Usually they are angular, but often are rod-shaped and resemble bacilli. A few cells containing fat droplets are occasionally seen at the periphery of the lobule. When, with increased accumulation of pigment granules occupy all portions of the cell body, basal as well as central, changes in the cell are demonstrable. The nucleus often presents evidence of degeneration. It is smaller, irregular in outline, with less nuclear material present, so that it remains as a pale shrivelled body, visible in some cases only with careful focusing of the microscope. Other masses of pigment granules maintaining the outline of liver cells contain no nucleus. Representing apparently the final stage of cell degeneration, a mass of pigment granules is found free in the tissue. No longer presenting the outline of a cell, it corresponds in size with the pigment accumulations found in those cells which are most intensely impregnated. Conspicuous in stained sections are groups of pigment masses, which, for the most part maintaining cell outlines, represent often ten or twenty cells, and stand out as pigment islands in sharp contrast to the well-stained liver cells adjacent.

In those cells whose protoplasm is almost wholly replaced by pigment much irregularity in the size of the granules is observable. Globules often the size of red corpuscles are found. With further evidence of cell degeneration the size of the globules increases, so that, when final disintegration takes place, there is liberated a mass of granules and globules resembling those found in great abundance in the fibrous tissue. Along the central vein, and following the strands of tissue radiating from it, are seen masses of pigment whose location indicates that they are transported, presumably along lymphatic spaces, from the interior of the lobule toward the central vein. Abundant accumulation of pigment exists in all parts of the interlobular tissue, both along the course of the sublobular veins and in the tissue about the portal spaces.

The adventitia and media of the hepatic artery and portal vein contain but little of the brownish-yellow pigment. The endothelial cells of the portal vein, however, contain a moderate amount, and within the lumen are seen large, flat, oval cells containing pigment granules. It seems probable that the majority of these are at least endothelial cells, which, after death, possibly in the process of hardening or cutting, have been dislodged from their normal position. The brownish-yellow pigment is not present in the endothelium of the hepatic arteries and in their lumen no pigment-containing cells are seen. Pigment is more abundant in the wall of the sublobular veins. Their endothelial cells contain it in abundance, and within their lumen are iron-containing cells resembling those found in the portal vein.

Newly formed bile-ducts are numerous in the interstitial tissue. Occasionally in the tissue about the central vein one sees several such structures represented by parallel rows of cubical cells. These ducts contain brownish-yellow granules in moderate amount. The epithelial cells of the larger ducts contain similar pigment.

The brownish-yellow pigment, whose location has been described, gives the microchemical reactions characteristic of iron. Treated with potassium ferrocyanide and hydrochloric acid it takes a green color. An aqueous solution of hæmatoxylon gives it a deep black. The reaction with potassium ferrocyanide and hydrochloric acid varies with the time of exposure and with the strength of the reagents. If sections are immersed for an hour to an hour and a half in equal parts of a 2 per cent. solution of potassium ferrocyanide and hydrochloric acid, one part to a hundred parts of water, all the granules within the liver cells assume a green color.

There is present a second less conspicuous variety of pigment, differing from that already described both in situation and in morphology. In certain cells in the media and adventitia of both veins and arteries are deposited fine, pale-yellow granules of almost uniform size. Some of the cells containing this pigment are elongated and spindle-shaped with rod-like nuclei, while others are large, irregular in shape, and provided with irregular processes. The first are apparently smooth muscle cells, the second connective-tissue cells. The latter are abundant in the walls of the ducts, in the tissue about the nerves, in the intervening tissue of the portal space, and as a conspicuous layer in the liver capsule a short distance below the serosa. The pigment in these cells does not give the microchemical reactions characteristic of iron, being unchanged by potassium ferrocyanide and hydrochloric acid. In sections stained with methylene-blue these granules take a blue, often bluish-black, color, and become very conspicuous. This fact was first observed by Buss.[8]

Areas of focal necrosis referable to typhoid fever are present. They may represent either a small number of necrotic cells or a considerable portion of a lobule.

Pancreas. Chronic interstitial inflammation is present. Bands of fibrous

tissue separate the lobules, which often stand out as isolated islands of parenchyma. Although the most marked increase of fibrous tissue is interlobular, there is here and there an invasion of fibrous strands between the acini. Pigment, giving the reactions of iron, is deposited in great quantity within the secreting cells, and is located, when moderate in amount, in that portion of the cell directed toward the lumen of the acinus—with greater accumulation all parts of the cell-body are occupied, and, as in the liver cells, globules of large size are then seen. Such a cell may have a palely staining nucleus of irregular outline or a nucleus may not be demonstrable. In the interstitial tissue the pigment is for the most part in groups of granules and large globules, varying much in size. These are apparently masses of pigment set free by the disintegration of cells. About such pigment round cells are often numerous. Pigment is frequently abundant in the cells composing the intertubular cell-groups or islands of Langerhans. These structures are present in moderate number. They have not, as a rule, their usual position within the lobule, being surrounded by fibrous tissue, which may contain much pigment. At times there is an increase of fibrous tissue along the capillaries penetrating them. Here and there in sections are seen areas which present a peculiar appearance. The cells of one or several lobules or a part of a lobule have lost the alveolar arrangement characteristic of the pancreatic parenchyma. At first sight it may be supposed that this disturbance of the usual structure is artificial in origin, produced possibly in cutting the section, but it has been observed in tissues hardened by a variety of methods and cut after embedding in both paraffin and celloidin. Moreover, the cells of such areas differ from those of the surrounding gland tissue. They are smaller and polygonal in shape. Their nucleus is often smaller and contains more chromatic substance than those adjacent. A conspicuous feature is the abundance of cells containing two nuclei, and at times three or even four are seen in the same cell. Mitotic figures have not been observed. The significance of these areas is doubtful; it is possible that they are the seat of cell-proliferation, and may bear some relation to the increased size of the organ.

Finely granular iron-free pigment, like that found in the walls of the hepatic bloodvessels, is present also within the cells of the same character in the walls of the veins and arteries of the pancreas. Pigment of identical characteristics is found in the walls of the larger ducts.

Heart. Well-marked fragmentation and segmentation of the myocardium is present. Brownish-yellow pigment is deposited in great quantity within the muscle fibres. It has the location of that which is present with brown atrophy of the organ, and, when moderate in amount, is accumulated in the neighborhood of the nucleus. All the pigment present does not give the reactions of iron, and in specimens treated with ferrocyanide of potassium or with aqueous hæmotoxylin a considerable amount of unchanged pigment remains. In sections of heart muscle treated with methylene-blue none of the pigment within the muscle-cells take the color observed when the iron-

free pigment of the walls of the hepatic bloodvessels is so treated. This pigment is apparently that which is found normally in the muscle fibre and is increased in the condition of brown atrophy. The pigment remaining unchanged after treatment with reagents which demonstrate iron is greater in amount than that normally present in the muscle fibres. In the interstitial tissue are seen here and there groups of globules of iron-containing pigment similar to those found free in the tissues elsewhere. The wall of the bloodvessels contain iron-free pigment staining with methylene-blue.

Gastro-intestinal Tract. The pigmentation of the stomach and intestine differs from that of the organs previously considered. Here the pale yellow, iron-free pigment predominates and gives macroscopic discoloration to the organ. Brownish-yellow, iron-containing pigment is fairly abundant in the epithelial cells of the cardiac glands, and is present in very small amount in the cells of the pyloric glands, while an occasional clump of granules is seen free in the tissue. The iron-free granules are in cells which have usually the character of smooth muscle fibres, although a few are apparently connective-tissue corpuscles situated between the muscle fibres or in the submucosa. The distribution of the pigmented cells varies in different parts of the gastro-intestinal tract. Throughout the stomach the muscularis mucosæ is pigmented. In the cardiac portion the circular and longitudinal layers are not so affected, while in the pyloric region there is in the circular muscle layer a conspicuous zone of pigmentation immediately below the submucous tissue. The walls of the arteries and veins of the submucosa contain pigment of the same nature. Throughout the small intestine iron-free granules are found in the cells of the muscularis mucosæ. A small amount of pigment is present in the circular muscle layer, but does not form the zone present in the pyloric portion of the stomach. In all parts of the small intestine pigment is most abundant in the cells of the longitudinal layer. The vessels of the submucosa contain numerous pigmented cells. Less pigment is present in the ileum than in the jejunum, while in the colon it is found in still smaller quantity, though it has the same location as elsewhere. The epithelium of the Brunner's glands of the duodenum are conspicuously impregnated with iron-containing pigment, the protoplasm of the cells being almost completely replaced by pigment granules.

Lymphatic Glands. Several lymph glands were examined. One of these was situated beside the inferior vena cava where it receives the hepatic vein. Lymphatic tissue is almost wholly replaced by masses of brownish-yellow pigment giving the reactions of iron, so that the organ is practically a mass of pigment surrounded by a thickened capsule and penetrated by a thickened fibrous septa. Among the pigment granules are scattered lymphoid cells, small groups remaining here and there. The pigment lying within the meshes of the reticulum is almost wholly extracellular, being in the form of particles which vary greatly in size, and resemble the extracellular pigment in the interstitial tissue of the liver, pancreas, and heart. It is apparently carried to these lymphatic glands along the lymphatic channels in the same

way that coal pigment is carried from the lung to the bronchial glands. An occasional fixed tissue-cell containing brownish-yellow granules is observed. In the smooth muscle and connective-tissue cells of the bloodvessels and in connective-tissue corpuscles of the capsule iron-free granules are found.

Spleen. The great engorgement of the bloodvessels and consequent tumefaction explain the fact that in spite of an abundant pigment deposit there is not the macroscopic pigmentation observed in other organs. Iron-containing granules are present in the branched reticular cells of the pulp and in the endothelial cells of the capillaries. Indeed, the capillaries on cross-section often form conspicuous rings of pigment-containing cells. In less quantity round and oval pulp-cells contain brownish-yellow granules. In the Malpighian bodies pigment is almost entirely absent, and when found occurs in clumps of irregular extracellular globules, resembling those so abundant in the lymphatic glands. Iron-free pigment is not abundant, but is found occasionally in the elongated connective-tissue cells of the trabeculæ.

Adrenal. Pigmentation is almost wholly limited to the so-called glomerular zone, which forms a sharply defined corona of brownish-yellow color immediately below the capsule. When moderate in amount, the pigment, which gives the characteristic reactions of iron, is situated in that portion of the cell most distant from the capillaries, but as a rule it is present in such quantity that all portions of the cell-body are occupied. Degenerative cell changes similar to those observed in the liver and pancreas are associated with the accumulation of pigment. The capsule in places is very slightly thickened and cellular, and contains globules of pigment, apparently set free by the disintegration of parenchyma cells. In the cell columns there is here and there a deposit of pigment granules.

Kidney. Pigment is present in very small quantity and is limited to an occasional tubule or glomerulus. Here and there the epithelial cells of a convoluted tubule contain pigment granules in great quantity, and differ from those of neighboring tubules in being of smaller size and more cubical. The glomeruli often contain pigment granules located apparently in the epithelial cells and occasionally there is a similar deposit in the loop of Henle. The bloodvessels differ from those of the organs more impregnated with iron in containing almost no iron-free pigment. An occasional cell thus pigmented can be seen, but search is required for its demonstration.

Lung. Pigment is scant. Occasionally within the alveolar septa are found brownish-yellow granules resembling the iron-containing granules in other situations. At times they completely fill an oval cell with an oval nucleus, while again they are extracellular. In many instances it is evident that these cells or free masses lie within the lumen of capillaries. Pigment-containing cells of a similar nature are seen in the larger vessels, and it is not inconceivable that in part at least they are endothelial cells of the liver or other organ, which, injured by pigment accumulation, have been dislodged from their position. Within the lumen of the larger vessels pigment granules are occasionally seen in round mononuclear cells very slightly larger than

polymorphonuclear leucocytes. Iron-free pigment is not found in the walls of the bloodvessels.

Skin. In the lowermost cells of the Malpighian layer there is a well-marked increase of the normal pigmentation. The granules here found do not give the reactions of iron nor do they stain with methylene-blue. In the cells of the sweat-glands are occasionally found iron-containing granules in small number, and between the tubules are connective-tissue cells containing similar pigment. Iron-free pigment is found in very small amount in the walls of bloodvessels of the subcutaneous tissue. Neither pigment granules nor pigment-containing cells are found within the lumen of the bloodvessels.

Testicle. The cells of the seminiferous tubules contain no pigment. Along the vessels in the angular interstices between the tubules are conspicuous groups of polygonal and oval cells completely filled with yellow granules, apparently the so-called interstitial cells, which normally contain a small amount of pigment. The endothelial cells of the vessels also contain conspicuous granules. The pigment of the interstitial cells remains unchanged after treatment with potassium ferrocyanide and hydrochloric acid, while that of the adjacent endothelium gives the characteristic reaction of iron.

Under the designation "hæmochromatosis," von Recklinghausen,[1] in 1889, described a condition of pigmentation affecting various organs. Brown pigment, which he thinks is derived from the hæmoglobin of the blood, is deposited within certain tissues and gives to them macroscopic pigmentation. Cases of intense wide-spread pigmentation had previously been described by Quincke,[2] Tillmanns,[3] and Hindenlang.[4] Cases of similar pigmentation, associated with diabetes and cirrhosis of the liver, had been described by Hanot and other French writers.

The anatomical picture of generalized pigmentation drawn by v. Recklinghausen is very clearly defined. Most of the glands of the body have a deep brown color and within their secreting cells are found reddish-yellow or ochre-colored granules. In the liver this pigment is present in the parenchyma cells and in Küpffer's cells. Michrochemical reactions prove that it contains iron. A second kind of pigment, distinguishable from the first by its occurrence in finer granules of pure yellow color, is found in the smooth muscle-cells of the stomach and intestines, of the bloodvessels and lymph-vessels, rarely in those of the urinary bladder, ureters, and vas deferens. It also exists in the connective tissue cells of certain localities—for example, Glisson's capsule, the splenic trabeculæ, and the sheaths of bloodvessels. This pigment does not give the reactions characteristic of iron. v.

Recklinghausen calls the iron-containing pigment "hæmosiderin," the iron-free pigment "hæmofuscin." The use of these names does not necessarily imply that we have any means of identifying these substances as definite chemical compounds or that we can recognize them when they occur in other situations.

v. Recklinghausen thinks that the hæmofuscin as well as the iron-containing hæmosiderin is derived from the hæmoglobin. In his cases of generalized pigmentation there was an associated cirrhosis of the liver.

v. Recklinghausen studied twelve cases which he regards as examples of local and general hæmochromatosis. Hæmochromatosis he apparently defines as a condition of pathological pigmentation due to the deposition of pigment derived from the blood. Such a definition includes a variety of dissimilar forms of pigment deposit; brown atrophy of the heart, for example, fulfils its conditions, since, as is believed, the ultimate origin of the pigment there found is the hæmoglobin of the blood. Nevertheless, it evidently has but little in common with the general hæmochromatosis already described.

There is, however, a local condition which has been associated with hæmochromatosis by several observers. I refer to pigmentation of the intestine caused by deposition of fine yellow granules in the smooth muscle-cells. Goebel[5] has made a careful study of this form of pigmentation. In adults a moderate degree is almost constant. The amount of pigment present bears a relationship to the age of the individual, so that with increasing age there is an increased pigment deposition. Other influences, however, may play an important part in producing the condition. With wasting diseases—for example, tuberculosis and carcinomatosis, there may be an accumulation equal to that present in advanced age. In sixteen of one hundred bodies studied by Goebel the pigment deposit was of sufficient magnitude to cause macroscopic discoloration, characterized by him as rust-brown. Hintze[6] has described two cases of similar intestinal pigmentation.

The pigment present in these cases does not give the reactions of iron, and agrees in morphology and location with the hæmofuscin of v. Recklinghausen. Hence both Goebel and Hintze conclude that this intense intestinal pigmentation represents the first stage of hæmochromatosis. Hæmosiderin is, however, not present, and is the hæmosiderin whose wide distribution forms the most characteristic

feature of general hæmochromatosis. Indeed, the iron-free pigment has apparently been overlooked in a number of cases of generalized pigmentation, whose description otherwise agrees with the picture drawn by v. Recklinghausen. It is, moreover, as will be shown, with the presence of this iron-containing pigment that are found marked pathological changes in the containing cells. The accumulation of pigment within the smooth muscle-cells of the intestine is apparently an accentuation of a physiological process, much more closely related to the brown atrophy of the heart than to general hæmochromatosis. v. Recklinghausen's description represents a condition, presenting no close similarity to any form of local pigmentation with which we are familiar.

The important features of this description are: 1. The presence in the epithelial cells of various glands, notably the liver and pancreas of an iron-containing pigment. 2. The presence of an iron-free pigment in smooth muscle cells of the gastro-intestinal tract and of the bloodvessels and lymph-vessels and in certain connective-tissue cells. 3. The association of cirrhosis of the liver with the pigmentation. To this condition, apparently a distinct pathological entity, the term hæmochromatosis should be limited, even though v. Recklinghausen, its originator, applied it to conditions of local pigmentation as well.

Prior to v. Recklinghausen's publication several observers had studied cases of wide-spread pigmentation. Quincke[3], in 1877, observed with anæmia a deposition of iron in various organs—notably in the liver and spleen, and in one instance found microscopic pigmentation of the liver and pancreas as a result of the iron deposition. Tillmanns[5] described brown pigmentation of the liver, of the abdominal lymphatic glands, and in less degree of the spleen and pancreas, in a man who two months before death had sustained a fracture of the pelvis and, the observer thought, a contusion of the liver. Hindenlang[4] observed in association with morbus maculosus Werlhofii pigmentation of the glands of the body, particularly the liver, which was slightly cirrhotic, and the pancreas, and in these organs found a pigment corresponding morphologically and in situation to that which v. Recklinghausen subsequently described as hæmosiderin. The presence of an iron-free pigment was not mentioned, but, being much less conspicuous than the hæmosiderin, it may readily have been overlooked, the gastro-intestinal tract not having received histological examination. Hintze[6] has described six cases which he regards as examples of hæmochromatosis. Several of them had previously been mentioned by Lubarsch.[7] Only three agree in detail with the description which v. Recklinghausen has given. Two are the cases of extreme intestinal

pigmentation before mentioned, and in a third, the case of an individual who five years before death had undergone an operation for the removal of a cyst of the pancreas, the deposition of iron-containing pigment was limited to the pancreas and neighboring lymphatic glands. The pancreas was the seat of a chronic interstitial inflammation with cyst formation, and the pigment was present only in the fibrous tissue, while the epithelial cells contained none. Although the intestine presented the variety of pigmentation described by Goebel, the condition cannot be regarded as hæmochromatosis, and was probably the result of local hemorrhage in or about the diseased pancreas. Buss[8] has described a typical case of hæmochromatosis associated with cirrhosis of the liver and diabetes mellitus.

Letulle[9] records two cases and Richardière[10] one in which, associated with hypertrophic cirrhosis, accompanied by very abundant hæmosiderin pigmentation, there was similar pigmentation of the pancreas and of other organs. In these cases pigmentation of the skin was apparently absent.

A condition, associated with hæmochromatosis by v. Recklinghausen, has been studied particularly by French writers. In 1882, Hanot and Chauffard[11] described two cases of diabetes mellitus associated clinically with hypertrophic cirrhosis of the liver and bronze-like pigmentation of the skin. At the autopsy upon the first of these cases was found cirrhosis of the liver, characterized by the presence of wide bands of connective tissue. In the liver cells, as well as in the interlobular bands, were brown pigment granules in great quantities. In the second case, more carefully studied, the liver and pancreas presented a brown pigmentation, and were the seat of advanced chronic interstitial inflammation, both parenchyma cells and interstitial tissue containing masses of pigment granules. The stomach and duodenum were of a bluish-black color and pigment in small granules was found below the serosa. Letulle[12] several years later reported two cases of a similar nature. In a second communication Hanot, in conjunction with Schachmann,[13] recorded a fifth case and reviewed those previously published. He believed that the observations previously made established the existence of a new form of cirrhosis, *cirrhose pigmentaire diabétique*, and of a new clinical condition, *diabète bronzé*.

The designation "diabète bronzé" has been in general accepted, but not without protest. Bronzing of the skin is not a consistent phenomenon, and has been found absent in one case of Letulle, in the case of Hanot and Schachmann, and in a case recorded by Brault and Galliard.[14]

In the recorded cases of so called bronzed diabetes,* as far as they

* The published cases of bronzed diabetes, numbering twenty-four, have been carefully collected by Anschütz, and certain data are presented in tabular form in his comprehensive review of the subject, which has appeared in the Deutsches Archiv für klinische Medicin, 1899, lxii. p. 411, subsequent to the preparation of this paper. For this reason a table of cases prepared by myself has been omitted.

are reported with sufficient detail, the symptoms and pathological findings are very constant. Clinically, the picture is one of a rapidly fatal diabetes mellitus associated with cirrhosis of the liver, usually of the hypertrophic variety. Bronzing of the skin is, as stated, not constant, but has been present in the majority of the cases. At autopsy has been found a deep pigmentation of the liver and pancreas associated with cirrhosis and in cases carefully examined macroscopically and histologically interstitial pancreatitis. An ochre-colored pigment, giving the microchemical reactions of iron, is present in the parenchyma cells of the liver, pancreas and other glands, in the muscle fibres of the heart, in the interstitial tissue of these organs, and in the lymphatic glands.

The facts relating to the incidence of the disease are of interest. No recorded instance of hæmochromatosis or of bronzed diabetes has occurred in the female. The age of the individuals affected with bronzed diabetes has varied between thirty-three and sixty-two years, the greatest number occurring in the fourth and fifth decades. The cases of simple hæmochromatosis fall within these limits. It has been believed that the disease is more common in France than elsewhere, and this is to a certain extent indicated by the fact that of twenty-four cases seventeen have been observed in that country. Simple hæmochromatosis has been, however, described more frequently by German writers.

The pathogenesis of the condition has been the subject of varied speculation. Hanot and Chauffard, and subsequently Hanot and Schachmann, have maintained that the primary etiological factor is the diabetes mellitus, that the diabetic alteration of the blood in conjunction with endarteritis, which they have found constant in their cases, causes a disturbance in the nutrition of the liver cells, an alteration of the pigment metabolism and a deposition of pigment within the cell-body. The excess of pigment so formed is reabsorbed by the capillaries, and diffused possibly in the form of emboli over the entire organism. Letulle,[12] finding the same process of pigment deposition in other organs—for example, the heart—that takes place in the liver, comes to the conclusion that the pigment is formed in the cells in which it is found from the hæmoglobin of the blood. He regards the diabetes as primary, and thinks that degeneration of hæmoglobin, wherever it exists, occurs under the influence of the hyperglycæmia.

Brault and Galliard[14] also give prominence to diabetes as the important factor in the production of pigmentation. The hæmoglobin of the diabetic is, they think, so altered that it is incapable of the normal transformation into bile pigment, and is deposited in the liver cell. Furthermore, it accumulates in the blood and wherever pigment is elaborated and utilized.

Hernandez[16] thinks that dissolution of hæmoglobin takes place under the influence of a general malady—diabetes—and pigment is deposited in the glandular cells, altering their nutrition and finally causing their destruction. The pigment is not eliminated but passes into the lymphatics, and causes in their walls an irritation, manifested by an increase of the connected tissue of the organ. Mossé[17] believes that under the influence of the hyperglycæmia pigment granules are formed within the bloodvessels at the expense of the altered or dissolved hæmoglobin. The pigment accumulation in the liver is in proportion to the specialization of the liver cells to a chromogenic function and to the large volume of blood which traverses the organ. The coexistence of hyperglycæmia and melanæmia contributes in very great part to the production of cirrhosis. De Massary and Portier[19] support the conception that a diabetic alteration of the blood is the essential etiological factor in the production of the pigmentation. Rendu and de Massary[20] advance the hypothesis that the pigment is deposited in the various cells of the body as the result of an abnormal action exerted by the cell upon the hæmoglobin of the blood, the alteration of metabolism being the manifestation of a general cachexia caused by diabetes associated with cirrhosis of the liver.

A second smaller group of writers think that the pigmentation is produced by a primary disease of the blood, that as a result of some fundamental cause there is an alteration of the blood and subsequent formation of pigment from the altered hæmoglobin. The relation of the concomitant diabetes and cirrhosis then remain to be explained. Buss suggests that the glycæmia may be the result of an incomplete oxidation of oxidizable carbon, resulting, in turn, from a diminished oxygen-carrying power of the altered hæmoglobin. P. Marie[18] thinks that there follows the action of some primitive cause a dissolution of the hæmoglobin, which is transformed by the protoplasm of various cells of the body into pigment deposited in them. The pigment in turn causes a degeneration and destruction of the cells in

which it is accumulated and consequently chronic interstitial inflammation of various organs, notably the liver. The bronzed diabetes is neither clinically nor pathologically the classic diabetes, but is a distinct morbid entity, as is, according to his belief, pancreatic diabetes; and if, he says, it should be necessary to compare the condition with any other, he would turn his attention to pancreatic diabetes. Acard,[21] Dutournier,[22] and Jeanselme[23] reiterate the conception of Marie, and suggest that perhaps the diabetes is only an accessory phenomenon which appears with a certain degree of chronic interstitial pancreatitis. Anschütz[15] has convinced himself that the diabetes finds its cause in chronic interstitial pancreatitis, which, like the cirrhosis of the liver, he believes, is a manifestation of an underlying condition.

The French writers who have described cases of "diabète bronzé" do no identify the pigmentation with the hæmochromatosis of v. Recklinghausen. In the very early cases no examination of the chemical nature of the pigment was made. Hernandez demonstrated that the brownish-yellow granules found by him in the epithelial cells of the liver, pancreas, and kidney, in the muscle cells of the heart, in the connective tissue of these organs, and in the lymphatic glands gave the microchemical reactions known to be characteristic of iron. In this and in subsequent cases the brownish-yellow pigment agrees in morphology and in location with the hæmosiderin of v. Recklinghausen. No mention is made by the majority of the French writers of an iron-free pigment present in smooth muscle cells and in certain connective-tissue cells. It is the absence of hæmofuscin alone which raises doubt as to the identity of the pigmentation of bronzed diabetes with hæmochromatosis. The hæmofuscin, occurring in fine pale-yellow granules within cells, is much less conspicuous than the more coarsely granular hæmosiderin, and may be very readily overlooked in specimens treated with reagents which demonstrate iron. Auscher and Lapicque[24] studied the pigment present in the case reported by Marie. In addition to widely distributed ochre-colored pigment, which became black on treatment with ammonium sulphide, they found on the intestinal wall a second variety of pigment, which was, according to them, of black color and dissolved in ammonium sulphide. Quantitative determination of the iron of the intestinal wall demonstrated a small percentage, while that of the liver was extremely large. The pigment observed by Auscher and Lapicque, and subsequently found by Acard

and Dutournier, though described as black in color, is apparently the iron-free hæmofuscin.

Buss, in an inaugural dissertation, as mentioned, reports a case of diabetes associated with cirrhosis of the liver and of the pancreas and with general hæmochromatosis. He finds the iron-containing and the iron-free pigment in locations corresponding to those mentioned by v. Recklinghausen. On the one hand, there is no reason to doubt that the pigmentation in this case is identical with that of hæmochromatosis, and, on the other hand, the case presents the clinical and pathological picture to which Hanot has given the name "diabète bronzé."

The case described by the writer holds a position intermediate between hæmochromatosis and the so-called bronzed diabetes. Associated with hæmochromatosis there is bronzing of the skin, cirrhosis of the liver of advanced grade, and chronic interstitial pancreatitis. Diabetes was, however, not present. It is evident, then, that the generalized pigmentation of bronzed diabetes is the hæmochromatosis of v. Recklinghausen.

When considering the etiological factors concerned in the deposition of great quantities of pigment in the liver and other organs we direct our attention to the blood, since it cannot be doubted that this iron-containing material is derived more or less directly from the hæmoglobin. It is well known that in pernicious anæmia, with active blood destruction, there is a deposition of iron within the liver and other organs, but pigmentation of the character under consideration is at least in the great majority of cases not found. A considerable proportion of the cases, both of simple hæmochromatosis and of hæmochromatosis associated with diabetes, have been accompanied by conditions which involve active destruction of the red blood-corpuscles. Hindenlang's case of general pigmentation, almost certainly one of hæmochromatosis, was associated with morbus maculosus Werlhofii. In four other cases purpuric eruptions have been observed. In several there have been local hemorrhagic conditions, as, for example, hemorrhagic pericarditis or peritonitis, as in cases of Hintze. In the case of Buss there was found at autopsy hemorrhagic pleurisy and peritonitis and hemorrhagic pachymeningitis. Other forms of local hemorrhage have been noted. The conditions cited present considerable variety, and in many cases were late manifestations in the disease. In many cases, moreover, local hemorrhages were not demonstrable. It is then

unnecessary to assume that the hæmoglobin forming the pigment arises from the destruction of red corpuscles of extravasated blood. It seems possible that, associated with some primitive alteration of the blood, there is a tendency to local hemorrhage, the hemorrhages being merely secondary manifestations of the same disease of the blood, which, associated with intravascular destruction of red corpuscles, precedes the pigment deposition.

In a case of Jeanselme, examination of the blood demonstrated the presence of a moderate grade of anæmia, but otherwise no marked pathological change of the blood was noted. Coagulation was not retarded.

Attempts have been made to reproduce experimentally the pigmentation found in human beings. Two methods have been employed: 1. The conditions of local hemorrhage are produced, for example, by injecting blood into the peritoneum. 2. Hæmoglobin is set free within the circulating blood by the use of toxic substances which cause destruction of the red blood-corpuscles. Auscher and Lapicque[25] and Meunier[26] have attempted by these means to reproduce the pigmentation of the internal organs found in bronzed diabetes. Auscher and Lapicque, by injecting blood into the peritoneum, caused accumulation of an iron-containing pigment in considerable quantity in the spleen but in very small quantity in the liver. In cases of hæmochromatosis, however, the liver is the prominent seat of pigment accumulation.

It has long been known that toluylendiamin causes a destruction of the red blood-corpuscles, large doses producing in dogs hæmoglobinuria. By the use of this substance numerous experimenters have caused the deposition of an iron-containing pigment in the liver and other organs. Meunier, attempting to reproduce in dogs the pigmentation of bronzed diabetes, succeeded by the repeated injection of small doses in obtaining an iron-containing pigment in moderate amount in the liver, lymphatic glands, spleen, and bone-marrow. The immense iron accumulation of hæmochromatosis, however, has not been reproduced, so that experiments have thrown but little light upon the pathogenesis of the condition.

The origin of the second form of pigment described by v. Recklinghausen, hæmofuscin, has been discussed at length by several writers who have studied hæmochromatosis. The data at hand are, however,

very meagre. If the hæmofuscin were derived from the hæmosiderin the two would be found side by side in the same cell, and v. Recklinghausen, therefore, thinks that the hæmofuscin is formed independently from the hæmoglobin or some soluble derivative present in the lymph. Lubarsch and Hintze believe the hæmofuscin to be elaborated from the hæmoglobin as the result of a specific activity of the smooth muscle-cells. Lubarsch injected defibrinated blood between the serosa and muscularis of the intestine of rabbits and obtained in the smooth muscle-cells yellow granules of an iron-free pigment, formed, he thinks, by the action of the cells upon the liberated hæmoglobin.

It has been pointed out that a pigment apparently identical with the hæmofuscin of v. Recklinghausen is present in adults in the smooth muscle-cells of the intestine under conditions which may be regarded as physiological, and, according to Goebel, increases with advancing age. In the sixteen cases of well-marked intestinal pigmentation without hæmochromatosis studied by him this pigment was not limited to the muscle of the intestine, but was found sparcely distributed in the smooth muscle-cells of the bloodvessels of the intestine, kidney, liver, and lung, in the smooth muscle of the bronchi, urinary bladder, and prostate. He observed similar pigment in the spindle-shaped cells of the splenic trabeculæ and in connective-tissue cells of the liver, submaxillary gland, and mesentery. It seems evident, then, that the hæmofuscin found abundantly with hæmochromatosis occurs under conditions which may probably be regarded as physiological. Undoubtedly this pigment may occur unaccompanied by a generalized deposition of the iron-containing hæmosiderin.

Certain other iron-free pigments existing in moderate quantity under physiological conditions have been in the case herewith described found increased. The iron-free pigment present in the heart muscle is greater in amount than that found under normal conditions. The interstitial cells of the testicle, normally containing pigment in moderate quantity, are loaded with pigment granules which do not give the reaction of iron. The pigmentation of the skin which has given name to the disease is caused by the presence in the deepest cells of the Malpighian layer of an iron-free pigment, apparently not differing from that found under normal conditions.

It seems probable, then, that the same conditions which cause the deposition of an iron-containing pigment in various cells of the body

favor the chromogenic metabolism of those cells which under normal conditions are capable of forming pigment. It may be pointed out, moreover, that hæmofuscin is present in considerable quantity in the walls of the vessels of the liver, pancreas, and lymph-glands, which contain hæmosiderin in great quantity, while in the vessels of organs like the kidney and lungs, in which is deposited very little iron-containing pigment, it is almost absent.

As already indicated, a majority of those who have studied cases of bronzed diabetes regard the diabetes as the essential etiological factor. v. Recklinghausen so explained his case of hæmochromatosis associated with diabetes. Without sufficient basis apparently an active blood destruction is assumed to be the result of the diabetic condition. In the ordinary form of diabetes, however, an accumulation of iron does not take place in the liver or other organs, as shown particularly in cases studied by Zaleski* and Kretz.† A case of diabetes associated with cirrhosis of the liver without pigmentation is recorded by Hanot and Schachmann. Similar cases in which pigmentation was not, at least, a conspicuous feature are mentioned by Hansemann and other writers upon diabetes. There is, moreover, as will be pointed out, reason to believe that the diabetes is secondary to the hæmochromatosis.

In the cases of bronzed diabetes the two prominent features in addition to the generalized pigmentation are diabetes and cirrhosis of the liver, and it is to this second factor that a number of writers have directed their attention in attempting to explain the pigmentation. It is to be recalled, moreover, that cirrhosis of the liver, usually of a less intense grade, has been present in the cases of simple hæmochromatosis. In all instances of hæmochromatosis, both with and without diabetes, the greatest pigment accumulation has been in the liver, and consequently a disturbed chromogenic function of that organ has suggested itself. It is conceivable that an iron-containing substance is deposited in the liver-cells as the result of their inability to accomplish the normal elaboration of bile pigments from the hæmoglobin of the blood. This altered metabolism may be the concomitant of the cirrhosis of the liver, then to be regarded as the primary etiological

* Virchow's Archiv, 1886, civ., 91.

† Beitr. zur klin. Med. u. Chir., Heft 15, Wien., 1896; Centralbl. f. allg. Path. u. path. Anat., 1897, viii., 620.

factor. If the pigment is formed in the liver, how does it reach other portions of the body? Is there evidence that the pigment is transported by the blood stream either as emboli free in the plasma or as granules enclosed within phagocytic cells? An occasional particle of pigment has been found in blood obtained by pricking the skin, but the objection has been urged that such particles may be derived from the pigmented cutaneous glands. The demonstration in sections of an occasional pigment granule in the lumen of vessels is by no means conclusive, since an impervious material may in cutting be carried into such position by the knife. The demonstration, as in the case described by the writer, of cells containing pigment granules within the lumen of vessels is in no greater degree proof that in this way pigment is disseminated from a single depot of formation. For it is not inconceivable that from soluble substances in the plasma pigment is elaborated in those cells in which it is found. Moreover, as has been pointed out, it is probable that a certain number of pigment-containing cells are endothelial plates desquamated before death as a consequence of the pigment accumulation or after death as a result of post-mortem change.

A study of the process of pigment accumulation in widely separated organs throws more light upon the seat of its formation. The glands I have studied most carefully are the liver, pancreas, adrenals, and glands of Brunner. When the pigment is in moderate quantity, it is present as relatively fine round granules occupying that portion of the cell most distant from the capillaries—that is, in acinous glands the portion of the cell next the lumen. With greater accumulation the whole cell body contains pigment granules, and finally almost the entire protoplasm is replaced by them. In cells so loaded with pigment the individual granules vary much, occurring as large round globules, often of greater size than a red blood-corpuscle. Changes may also be observed in the nucleus of the cell. It becomes smaller, its outline often becomes irregular, and it assumes a shrivelled appearance. In cells appearing to be a mere mass of granules and globules of pigment, with careful focussing a very faintly staining vesicular nucleus is occasionally seen, while more frequently are found pigment masses without any trace of nucleus, but still maintaining the cell outline. Finally, the cell outline is lost and a clump of pigment particles of very variable size lies free in the tissue. The same process, observed

in the liver, takes place in the pancreas and adrenal gland, and, indeed, in the muscle-cells of the heart. It is, therefore, improbable that the pigment they contain is transported as emboli or in phagocytic cells from some distant organ—as the liver. Much more probable is it that the same process is taking place simultaneously in all the organs concerned, that the pigment is elaborated by the cells in which it is found from iron-containing material dissolved in the surrounding lymph.

Although, as it appears, the liver is not the seat of formation of the pigment found in other organs, a disturbance of the chromogenic metabolism of its cells may be an important factor in causing the deposition of pigment elsewhere. It may be that iron-containing derivatives of the hæmoglobin are not eliminated in consequence of changes in the liver-cells and so accumulate in the blood. The extreme pigmentation of the liver, greatly exceeding that of other organs, may hold to its chromogenic function some relation which our present knowledge of iron metabolism does not explain.

Doubtless, for the production of a condition of hæmochromatosis, some factor is necessary beside the mere disintegration of red corpuscles and setting free of hæmoglobin. Its absence in conditions associated with blood destruction sufficiently proves this point. Of a series of cases of cirrhosis of the liver studied by Kretz* in about one-half was found a moderate accumulation of an iron-containing pigment resembling hæmosiderin. He comes to the conclusion that the toxic matter circulating in the blood causes a degeneration of the liver-cells and at the same time acts injuriously upon the red corpuscles. It is the association of the two conditions which simultaneously produces cirrhosis and pigmentation. Possibly in hæmochromatosis the toxic material causing the blood destruction is of such a nature that it acts injuriously upon the cells of the liver and other organs so that they transform the soluble blood pigment reaching them into the insoluble hæmosiderin. Alcohol may, under certain conditions, have this action. Such speculations merely indicate the complexity of the conditions which underlie the generalized pigmentation.

Degenerate cells overloaded with pigment are in the case studied very abundant and can be readily demonstrated without prolonged search. We have thus an efficient factor for the production of a

* Loc. cit.

chronic interstitial inflammation. Newly formed fibrous tissue invades the lobule along the central vein and in places sends out fine radiating bands along the capillaries between the columns of liver-cells. The fibrous tissue about the central vein and that between the lobules contain large quantities of pigment for the most part extracellular as a result of the degeneration of the cells in which it was formed. This pigment lies free in the tissue presumably transported along lymphatic channels. When it is massed in large quantity there is usually evidence of active cell proliferation. In general the interlobular tissue is poor in cells, but in such areas proliferation may be indicated by the presence of small round cells. Two factors are, I believe, active in producing the scleroses: 1, pigmentary degeneration of the parenchyma cells; 2, irritation produced by the presence of the pigment in the interstitial tissue.

In the case I have described the pancreas is the organ, next to the liver, most conspicuously pigmented. Extreme pigmentation and consequent degeneration of the parenchyma cells can be readily seen. Fibrous septa deeply pigmented separate the lobules and in places strands of similar nature penetrate between the acini. The pancreas has been very superficially examined in many of the reported cases of bronzed diabetes, but in those in which a description of the microscopic appearance is given it is evident that chronic interstitial pancreatitis existed. The fact that the organ in the great majority of cases has not been found atrophic has probably, in certain instances, prevented the recognition at autopsy of interstitial inflammation. In but two cases apparently has it been found to be smaller than normal, while it is frequently described as voluminous, enlarged or normal in size. In seven cases the weight is recorded; the mean of the figures given, varying between 95 and 195 grammes, is 125.7 grammes, about one-half greater than the normal weight of the organ. The average weight of the liver, recorded in thirteen cases of bronzed diabetes, is 2497 grammes, and we must regard the condition present as a form of hypertrophic cirrhosis. The lesion of the pancreas differs from the more commonly observed form of chronic interstitial inflammation, accompanied by more or less atrophy of the organ and may be designated as hypertrophic pancreatitis. In my case, without diabetes, the pancreas weighed 170 grammes, almost twice the normal weight, and was the seat of an interstitial inflammation of moderate intensity.

The etiological relationship of chronic interstitial inflammation of the pancreas to diabetes has been well established in recent years by Hansemann and others, though the exact character and degree of such inflammation necessary to the production of glycosuria has not been definitely determined. Finding, with bronzed diabetes, chronic interstitial pancreatitis constant as far as we are able to judge, it is hardly possible to doubt that the diabetic condition is pancreatic in origin and makes its appearance when the pancreatitis has reached a certain grade of intensity. In the majority of cases the symptoms of onset are those of diabetes—that is, the individual is apparently in good health until the onset of glycosuria. In the three cases of hæmochromatosis without diabetes described by Hintze, diseases having no apparent relation to the hæmochromatosis caused death. In the present instance intercurrent typhoid fever caused the death of the individual before chronic interstitial pancreatitis had reached a sufficient grade of intensity to produce glycosuria and thus the hæmochromatosis was prevented from reaching its usual termination, pancreatic diabetes.

CONCLUSIONS.

1. There exists a distinct morbid entity—hæmochromatosis—characterized by the wide-spread deposition of an iron-containing pigment in certain cells and an associated formation of iron-free pigments in a variety of localities in which pigment is found in moderate amount under physiological conditions.

2. With the pigment accumulation there is degeneration and death of the containing cells and consequent interstitial inflammation, notably of the liver and pancreas, which become the seat of inflammatory changes accompanied by hypertrophy of the organ.

3. When chronic interstitial pancreatitis has reached a certain grade of intensity diabetes ensues and is the terminal event in the disease.

I desire to express my obligation to Dr. Welch and Dr. Flexner for the interest they have shown in the foregoing case and for the assistance they have given me in its study.

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DISCUSSION.

DR. OSLER: I have brought over, for your inspection, a patient in all probability illustrating this condition. Hanot's cirrhosis is characterized by the chronicity of the disease, the non-alcoholism, the large size of the

liver and spleen, and the absence of ascites except toward the close. The cases may last from three to thirteen years, may remain in fairly good health, and usually die from symptoms of toxæmia, which is a terminal infection. Of a number of cases of hypertrophic cirrhosis that we have observed during the past few years, two have presented this peculiar condition. This man came to the clinic two years ago and the probable diagnosis of Addison's disease was made. I did not see him at that visit. He is a man of good family history, not a drinker, has been in one position as a pilot for fourteen years, and he noticed about four years ago that he had begun to change in color. Since that time the only two features he has presented have been the increasing bronzing of the skin and recurrent attacks of purpura. He is a vigorous, healthy man, not very well nourished, and on examination last Saturday I found a well-marked hypertrophic cirrhosis with enlargement of the spleen. He has the long duration of the disease, the bronzing of the skin, the enlarged liver and spleen, and he has had the recurring hemorrhages which are so common, of course, in the true hypertrophic cirrhosis of Hanot's, and which are mentioned in a number of these cases reported in the German *Archives*. The skin has not yet been examined, but the urine shows the presence of iron and no sugar. [Exhibiting patient.]

DR. ADAMI: The case referred to by Prof. Welch was communicated by Dr. James Stewart and myself at a meeting of the Montreal branch of the British Medical Association, on May 6, 1898, but has not as yet been published in any journal, although I have referred to the case in an article on "cirrhosis" in the second volume of *Sajous' Annual*, 1898. Our neglect to do so has been mainly due to the fact that upon the study of further sections I became convinced that a change had occurred in the material in consequence, apparently, of the action of formalin upon the tissues. I had placed portions of the liver and pancreas in absolute alcohol, but the majority of the tissues had been placed according to our usual routine method (in formol-Müller), and upon comparing sections of the liver that had been hardened in these two preservatives we found, without doubt, that the hæmosiderin was either being slowly dissolved out or becoming more fixed in the latter; hence, I became a little dubious as to whether the results we obtained with certain tissues were absolutely correct, and delayed publication in order to make a fuller study of this disturbance.

I do not know that any one has as yet called attention to this action of formalin upon iron or iron containing pigment in the tissues. Apparently there is some liability for the formalin to act on the iron, so as to produce a soluble formate. Dr. Maude Abbott is studying further these specimens, and will later publish a full account of this case, with a study of the deposit of iron-containing pigment in the tissues.

Briefly, the case was that of a female of fifty years, unmarried, admitted to the Royal Victoria Hospital of Montreal, under Dr. Stewart, in July, 1897. For upward of ten years she had taken a glass or two of undiluted gin daily,

though recently beer had replaced the gin; for years also she had been in the habit taking soda and vinegar two or three times daily.

Two years before admission the present illness began, with symptoms pointing to gastric irritation. Upon admission, she was poorly nourished, the conjunctivæ were icteroid, while the skin had a dark slaty or bluish-gray color, both in the exposed parts and those covered by the clothing. There was a soft blowing systolic murmur at the apex over the aortic area and a marked degree of general arterio-sclerosis. There was evidence of effusion in both pleural cavities, more especially into the right, while she expectorated a scanty brownish sputum. The abdomen was fuller than normal; she complained of a sense of weight in the epigastrium and frequently vomited after meals. In the epigastrium was a firm mass having a raised convex surface and well-defined borders, the movements of which during respiration were synchronous with those of the liver. The gall-bladder could not be palpated; the spleen was markedly enlarged and reached to two and one-half inches from the anterior superior spine.

On several occasions the chest was aspirated and a few ounces of blood-stained serum removed. The urine at no time presented abnormal characters, save that on a few occasions a trace of albumin could be detected; *although frequent tests were made for sugar, this was never found to be present.*

During her stay in the hospital her general nutrition improved very considerably, more especially after treatment on the surgical side for suppurative otitis media with mastoid abscess. The pigmentation of the skin, however, underwent a definite increase, although it varied somewhat from day to day. This pigmentation was so marked that the patient was known throughout the hospital as "Blue Mary." She frequently complained of epistaxis.

Upon April 15, 1898, she suddenly became worse, passing into a semi-stuporous state and refusing nourishment; she died quietly on the following day. The cause of the sudden change and of her death could not be determined during life, for she neither vomited blood nor was there melæna. Diagnosis varied during life between malignant disease in the epigastric region, affecting either the liver or the pancreas, and hepatic cirrhosis.

The autopsy, performed eighteen hours after death, showed the exposed parts of the body to be of a curious ashen or bluish-gray color; the other parts had the same color, but to a less extent. The skin of the face was rough; that of the palms and hands singularly smooth, almost silky to the touch.

Taking first the abdomen, we remarked that there was complete absence of ascites, and again there were several richly vascular bands of omental adhesions to the parietes in the right lower quadrant of the abdomen; the stomach was greatly dilated and of a slaty color, and the coils of the small intestine were full and of the same slaty color. The right lobe of the liver was almost entirely covered by the ribs, the relatively large left lobe forming the main visible portion. It was this that had formed the mass palpable during life; the visible surface of the organ was distinctly of the hob-nailed type.

On removing the organs the stomach contained abundant black blood and gas; the first few feet of the jejunum were greatly distended with blackish fluid blood; below this the small intestines were relatively empty but blood-stained to within a foot of the valve. There was again more solid coagulated blood, and this also filled the colon right down to the rectum. Clearly death had been from hemorrhage into the alimentary canal, and the seat of the hemorrhage was found at a point not quite one inch above the cardiac orifice of the stomach, along the posterior median line of the œsophagus. Here pressure upon one of the projecting varicosities of the submucous veins led to the free oozing of blood out of a small depression or ulcer.

The liver was of normal weight—1550 grammes, or about 51 ounces; on the whole it was rather smaller in dimensions than normal; there were extensive adhesions in the shape of well-formed vascular fibrous bands between the right lobe and the diaphragm. On section the organ was dense, firm, and presenting everywhere small islands of liver-tissue of dirty yellowish color, surrounded by more bluish-gray, glistening fibrous tissue, which was present in great abundance.

The spleen was of great size—720 grammes, 23.3 x 13.5 x 4 cm.; the organ was flabby and on section pale and pulpy. The pancreas was long, thin, and moderately congested.

The suprarenals were of dark color with softened medulla; the kidneys relatively large, somewhat congested, presenting a condition of a mixed nephritis. There were adhesions between the atrophied uterus, rectum, and right ovary; and in the uterus several small fibroids—submucous, intramural, and subserous.

With regard to the head, the brain presented no abnormality; the membranes were healthy. There were generalized veil-like adhesions over the right lung and similar adhesions between the diaphragm and the base of the left. In the lungs themselves there was no evidence of tuberculosis, unless a minute, somewhat branched or spiculated calcareous body, toward the apex of the right lung, represented an obsolete tubercle rather than a small broncholith. The heart was relatively large, the valves all healthy, the muscle somewhat flabby, the left ventricle relatively thin-walled, the average diameter of its muscle being 9 mm. There were no signs of pericarditis.

MICROSCOPICALLY. Sections of liver showed appearances practically identical with those described by Prof. Welch; the bands of new fibrous tissue were, in general, large and generally sharply defined. The area of parenchyma enclosed varied in size, and there was well-marked absence of proliferated bile canaliculi; there was little evidence of compensatory hypertrophy of the parenchyma. Upon subjecting to Perl's test, iron-containing pigment was found present in extraordinary amount; this was present in all parts of the liver, in the endothelium of the portal vessels, in the dense clumps and tracts in the new connective tissue, and again abundantly in the liver cells themselves. The peripheral cells of the lobules were, in general, richest in pigment; here and there the deposit affected all the cells to the very centre of

the lobule. Not even in advanced cases of pernicious anæmia have I met with so extensive a deposit of hæmosiderin. In addition to this there was relatively abundant brownish pigment not converted by the ferrocyanide, evidently hæmofuscin.

With regard to the other organs, the only lymphatic glands kept were those situated on the posterior wall of the cardiac end of the stomach and beginning of the œsophagus; these were crowded with pigment mainly of the dark-brown type. The pancreas showed some fibrosis, distinct, but not very extensive, but the blue pigment showed remarkable distribution; it appeared to be mainly within the gland cells. Curiously, the most extreme pigmentation appeared to be in the outer portion of the gland; the cells of the more centrally situated alveoli showed extensive granular deposit of yellow-brown pigment with only occasional blue granules. The blue and brown pigment granules were of identical size and situation, and from the curious arrangement I can only conclude that at the periphery the iron was relatively unstable and so reacted to Perl's test, whereas, at the more centrally situated cells, it was more deeply fixed. For it must be kept clearly in mind that Perl's test acts only when the iron is in loose combination.

The heart-muscle showed some fibroid degeneration with congestion. Stained by ordinary methods the fibres appeared to show a condition of advanced brown atrophy; by Perl's test the granules took on the blue stain.

Other regions showing deposit of the pigment were the walls of the œsophagus and first part of the stomach. Here the endothelium of the vessels and the various non-striated muscle-fibres in the sections did not give the blue reaction, but presented abundant brown and very clearly defined granules. Unfortunately the rest of the stomach and intestines were not kept, the slaty color of these organs having been at post-mortem attributed purely to the extreme hemorrhage which had taken place into these viscera.

On the other hand, to our surprise, the spleen showed singularly little deposit of pigment; only individual cells here and there, which we took to be leucocytes, were crowded with granules giving the blue reaction. Similarly the kidneys were almost entirely free from reaction. At most, within the vessels here and there could be seen nucleated cells taking on the blue stain.

The skin also gave but a poor reaction. In the papillæ of the cutis were large cells which took on, more especially, the brown stain, and there was only a mere bluish reaction on the part of the lowest layer of the rete Malpighii.

As already stated, the action of the formalin upon the tissues may to some extent explain the failure to obtain a reaction in these organs.

By more extensive action with warm, dilute hydrochloric acid Dr. M. E. Abbott has been able to loosen the iron in a large portion of the pigment and thereby to gain Perl's reaction. By this means she has shown that this iron-containing pigment is found in greatest amount in the lymphatic glands of the abdomen, liver, pancreas, and heart-muscle, while the kidney is almost entirely free from it; the suprarenals contain it only in the outer portion of

the cortex, and that irregularly, while the spleen contains but a relatively small amount.

With regard to the meaning of this remarkable condition of hæmochromatosis I find myself a little at variance with Prof. Welch, for I can scarcely regard it as a morbid entity. So far as I can see, quite a fair number of cases of cirrhosis of the liver, upon careful examination, show the existence of a moderate increase in the amount of iron-containing pigment in the liver. While, if I read Hintze aright, the deposit is by no means associated with cirrhotic changes in the liver and pancreas, and may be found in connection with other abdominal disturbances, I freely confess that it is only in connection with the hepatic and pancreatic cirrhosis that it occurs to an extreme degree.

In the very early stage the deposit is confined to the coats of the small intestines, more especially to the muscular layers.

Not to enter too fully into discussion upon the subject, I am led to think that the origin for the condition is to be ascribed to disturbances occurring along the intestinal tract, and it is more especially in the walls of the intestine and the intestinal vessels that those changes occur which lead to the breaking-down of the red blood-corpuscles and the liberation of their iron-containing pigment.

Dr. Welch: Dr. Adami gives us the only case on record which has occurred in a woman. Purpura has occurred only in a small minority of the cases, and the real question as to whether this conception of it as an independent disease is the correct one is, of course, an open question, but that is the conclusion to which Dr. Opie has come.

THE SYMPTOMATOLOGY OF TUMORS INVOLVING THE HYPOPHYSIS CEREBRI.

By JAMES STEWART, M.D.,
OF MONTREAL.

It is generally recognized that tumors of or involving the pituitary body may, in addition to the results arising from local or general cerebral pressure, induce symptoms directly due to destruction or interference of the function of this structure. It is generally admitted that the hypophysis is either enlarged or diseased in every case of acromegaly. What relation the changes in the pituitary body bear to the acromegalic symptoms is, however, still a matter of speculation.

A number of cases of tumors involving the destruction of the hypophysis have been reported, chiefly by Weir Mitchell, Drs. Anders and Cattell, and Guy Hinsdale, where no symptoms of acromegaly were present. This paper is chiefly a record of two cases of a similar character, in neither of which were there any symptoms of acromegaly. In one case the symptoms, in addition to the direct cerebral pressure-signs, resembled a mixture of myxœdema and pernicious anæmia, while in the other the symptoms were those of a somewhat rapid infiltrating neoplasm of the anterior part of the base of the brain.

Case I. *Perithelial Angiosarcoma of the Pituitary Body. Symptoms: Headache, vomiting, and temporal hemianopsia; finally infiltration of the growth into the ethmoid and sphenoidal cells, causing hemorrhage from the nares; no symptoms of acromegaly or other forms of nutritional disturbance.*—Miss K., aged thirty-five years, a miniature painter, was admitted December 2, 1898, complaining of headache, dimness of vision, and occasional vomiting. She says that the headache and dimness of vision have been troublesome for upward of eighteen months. The failure of vision was noticed first in the left eye, and she observed that the pupil of this eye was larger than the right. Three months previous to admission the sight of the right eye was found to be also

failing, and the pupil of that eye becoming larger. The vomiting which occurs about every month, lasting from one to three days, was first noticed March, 1898.

She was born in Eastern Ontario, and always lived there, except for a period of six years, when she resided in the State of Illinois. With the exception of measles and whooping-cough there is no history of any illness. She has four brothers and five sisters living, all in good health. One brother died from pulmonary tuberculosis, and a sister from heart trouble. She was much worried for months previous to the onset of headache and dimness of vision, and had been treated for nervous prostration.

Present Condition. She is a tall and well-nourished woman, thirty-five years of age. She is able to walk about, but prefers lying in bed on her back, as in this position she suffers less from headaches. She is more than ordinarily intelligent, her mental state on admission being, as far as she herself or others could judge, fully normal.

Headache. Pain in the head is her great complaint. It is referred chiefly to (1) the left temporal and parietal regions; in the left eyeball and over the left brow; (2) to the occiput, just below the occipital protuberance, shooting downward and often forward, on both sides, often entirely circling the neck. The pain, she says, is continuous, but it is frequently intensified, especially on movement, on percussion, and at times spontaneously.

Dimness of Vision. Three months before her admission into the hospital Dr. Stirling had an opportunity of examining her eyes and found the following conditions present:

Right Eye. 5-9, outer half of the field gone, light perception reduced 5 degrees. The pupil active to light and accommodation, but indirect action from left eye lost.

Left Eye. Light perception reduced 8 degrees. She is able to count fingers at two feet in the lower and outer part of the field, but nowhere else. Pupil is 7 mm. in diameter, immobile to light and accommodation. There was a slight non-paralytic divergence.

There was simple atrophy of both optic nerves, without any diminution in the size of the large vessels.

Three months afterward Dr. Buller found a more advanced condition of atrophy, there being just perception of light in the left eye, and a marked diminution now all over the right field. He also reports a state of simple atrophy without diminution of the large vessels. The diminution of light perception in the right eye was so marked that he was not able to map out the field.

Her voluntary power is not in any way impaired. Nutrition is good. The knee-jerks are much diminished, while the superficial and organic reflexes are normal. There is no disturbance of any form of the muscular sense. The general sensibility is not in any degree impaired, and with the exception of the disturbance in the functions of the optic nerves already referred to, the special sense-nerves are normal.

Menstruation began when she was thirteen years of age and continued one year, when it permanently ceased.

The urine had a sp. gr. of 1025, contained ½ per cent. of albumin, together with numerous granular and hyaline casts.

The subsequent course was characterized by more or less continuous and severe headache, by occasional vomiting, and gradually increasing stupor. A few days previous to her death, January 7, 1899, there was a discharge of a bloody fluid from both the anterior and posterior nares. The immediate cause of death was hyperpyrexia.

I am indebted to Dr. A. G. Nicholls, Assistant Pathologist to the Royal Victoria Hospital, for the following account of the post-mortem.

In addition to the morbid changes met with in the brain, the following were found:

There was a subacute diffuse nephritis in both kidneys. The uterus infantile in type, being only 5.25 c.m. long. The ovaries were small, fusiform in shape and without noticeable scarring, and slightly fibroid.

The Brain. The calvarium was normal. The dura was thin, showing the convolutions of the brain through its substance. It was congested and exuded blood. The convolutions were flattened on both sides, chiefly over the vertex and posteriorly. The frontal convolutions appeared to be normal. There was considerable exudation of clear fluid about the base of the brain.

On removing the brain a tumor-mass was found at the base, lying in the sella turcica, and occupying the site of the pituitary gland, of which no vestige could be seen. The tumor measured 5 c.m. long by 4.75 c.m. broad. The upper surface was lobulated, forming grape-like masses of a reddish, translucent color, of soft consistence, and hemorrhagic appearance. There were two large lateral lobes, with three smaller ones anteriorly. The under surface of the tumor was very soft and diffluent, of the appearance of raspberry-jelly. This was probably due to manipulation. The tumor lay in the median line with a tendency to the left side. There was an oval excavation on the base of the brain in which the mass rested. The sella turcica was greatly enlarged in all directions, corresponding to the main mass of the tumor below. The body of the sphenoid was eroded from pressure, the bone being as thin as paper. The sphenoidal and ethmoidal cells contained a jelly-like mass similar to the tumor. The posterior nares contained blood-stained mucus. On the left side in front the tumor passed beneath the dura of the cranial base, reaching along the lesser wing of the sphenoid as far as the back of the left orbit. It had not, however, invaded the orbit. The growth had reached the top of the pharynx without causing any perceptible bulging. The tumor pressed directly upon the optic commissure, which was flattened. It reached backward to a point 2 c.m. anterior to the pons, compressing the left crus. Other cranial nerves seemed not to be directly involved.

The specimen was hardened in bulk, formol-Müller.

At closer inspection the mass was found to be bounded, at least above, by

a thin fibrous membrane, presumably the pia mater. Several sections were made through its substance, and through the optic chiasm, pons, medulla, left crus and cord.

Microscopically, the tumor was found to be inclosed in the upper surface by a laminated fibrous tissue membrane, presumably the pia mater. The finer structure of the mass varied somewhat in different parts. In the main it consisted of delicate capillary bloodvessels with elongated cells having oat-shaped nuclei. The bloodvessels were composed of basement membranes lined with flat endothelial cells; they were for the most part small, but in a few instances formed actual cavernous sinuses. The elongated cells were arranged about the bloodvessels, their long axes being placed radially to the centre of the vessel. This gave the tumor the appearance of being formed of a series of rings. In other places the elongated cells formed long, finger-like processes running in various directions and without the same definite relationship to the vessels. On the under surface of the tumor small spicules of bone were seen, showing that the new growth had forced its way through the body of the sphenoid. At the margin of the growth two or three very cellular nodules were seen which had a close resemblance to round-celled sarcoma. On the whole, as the tumor was composed largely of short, spindle cells, it had the appearance of a sarcoma, and owing to the relationship to the vessels, it must have started from the perithelium. No remains of the pituitary body were seen, nor was colloid present.

Diagnosis. Perithelial angiosarcoma of the pituitary body.

Sections through the optic chiasm showed that the optic nerves were in a state of extensive degeneration, the myelin sheaths being broken up and reduced to globular masses. The bloodvessels were distended, and surrounding them were masses of small, round cells.

Sections through the pons, medulla, left crus, and cord showed nothing abnormal.

The symptoms in this case extended over a period of about twenty months, and were clearly indicative of a cerebral growth in the neighborhood of the optic chiasm. There were no symptoms whatever of acromegaly, myxœdema, or pernicious anæmia. I would like, however, to call attention to two changes which have been frequently met in cases of tumors involving the pituitary body. These are cirrhotic changes in the kidneys, uterus, and ovaries. Boyce, in his valuable paper on hypophyseal growths, gives details of at least four cases where the kidneys were found to be granular.

CASE II. *Endothelioma of the base of the brain, causing pressure on the chiasma and obliterating the pituitary body; symptoms of a cerebral growth extending over nine years; right temporal hemianopsia; profound anæmia; a general appearance not unlike that seen in myxœdema; no changes in the osseous tissues.*

—Mr. W., a merchant, aged forty-two years, came first under the observation of Dr. Stirling in February, 1888, complaining of failing vision, headache, and vertigo. He first noticed the failure in vision in the left eye two years previously, and this was, I believe, the first evidence of any intracranial trouble.

He had been for a number of years and up to the time of the appearance of his present complaints a heavy drinker. There was no history or evidence of tuberculosis or syphilis. He complained of a dull frontal headache, but neither at this period nor at any time during the prolonged course of his illness was headache a prominent symptom. In walking he more or less constantly had what he called a giddy sensation, with a tendency to fall forward. Vomiting of a cerebral character was present for some months during the early period of the disease. Dr. Stirling's examination of the eyes revealed the following changes:

Left Eye. There is no perception of light. The pupil is semi-dilated and immobile, but reacts on stimulating the right eye with light.

Right Eye. Complete blindness to the outer side of the field. The inner side was amblyopic; vision being reduced to counting fingers at twelve feet. In reading type he is able to pick out a letter of the largest size (No. 16) here and there. In this area the perception of green was found to be very defective, and after looking at green for some time there was an after-image in pink.

Examination of the fundus revealed in the left eye white atrophy of the disk, with somewhat contracted vessels. In the right eye the disk is pale.

There was no objective disturbance of either sensation or motion. He complained, however, of numbness in the hands. He had frequent flushings, followed by profuse perspirations about the head and neck. The knee-jerks were slightly exaggerated, but the superficial and organic reflexes were normal.

The further course of this case was very slow, six years elapsing before his death, in 1894. His sight entirely failed in August, 1889. He became very fat and anæmic. The face and extremities were puffy, but in no part was there pitting on pressure. The puffy, pale skin presented a very striking clinical picture. The pallor of the skin was noticed when he first came under observation in 1888, but it steadily increased. In 1892 he presented the typical appearance of a person suffering from pernicious anæmia. The skin having a typical lemon-yellow tint, while the general state of nutrition appeared to be unusually good. In March, 1893, Dr. Gunn examined the blood. He found 2,800,000 red cells and the proportion of white to red as 1 to 1500. The red cells were irregular in size, microcytes being abundant; no nucleated red cells were found. Four months later a second examination of the blood was made by Dr. Gunn. He found 2,100,000 red cells, and the proportion of white to red as 1 to 1600. The urine was free from both albumin and sugar.

The anæmia remained up to death, but did not present any changes differ-

ent from the last above-recorded examination. His appetite remained good, and was even at times voracious. He was annoyed with photopsia, and during the last two years of his life he complained more or less constantly of hallucinations of vision, smell, taste, and hearing, and of general sensibility. He often imagined that burglars were breaking into the house, maintaining that he not only heard but saw them. He kept a revolver under his pillow, to punish any burglar who would attempt to come near him.

He frequently made mention of what he called "beasties" crawling over his skin, and would stoutly maintain that he not only felt but saw them. This was when he had no perception of light in either eye. Although his general nutrition and strength were fair, he spent almost the whole of his last year in bed. When urged to get up, he would make answer that he would do so the following day.

Summary of the symptoms and course:

1. Gradual loss of vision in both eyes, going on to total blindness in the left and to temporal hemianopsia in the right, followed later on by total extinction of the perception of light.

2. There was complaint in the earlier months of his illness of frontal headache and of occasional vomiting.

3. The presence of more or less constant giddiness throughout the course of his disease, with a tendency at first to fall forward and afterward to one side.

4. Profuse intermittent flushings and perspirations about the face and neck, but the skin of other parts was dry and harsh.

5. Slow cerebration, as evidenced by a slow, drawling speech and slowness in answering questions. There were also great apathy and drowsiness and lowered temperature.

6. Hallucinations of sight, smell, of hearing and of general sensibility.

7. A very pronounced lemon tint of the skin, resembling in this respect the appearances considered to be characteristic of pernicious anæmia. The blood changes corresponded also to those met with in pernicious anæmia.

8. Œdematous-like condition of the hands and feet, but no pitting on pressure.

9. During the last two years of his life he kept his bed more or less constantly, taking little or no interest in anything, but still able to talk and answer questions intelligently. He finally died in a state of coma.

Diagnosis. The general symptoms—headache, vomiting, vertigo, and optic atrophy—pointed clearly to a cerebral tumor, while the temporal hemianopsia localized this to the optic chiasm. Had the visual disturbance been seen earlier it is highly probable the limitation of the field would have been met in both eyes. The absence of the pupillary reflex indicated that the lesion must have been situated between the left eye and the basal optic nuclei. Further, the optic atrophy showed that the lesion could not be further back than the basal nuclei, as in lesions of the optic radiations or cortex, white or essential atrophy is exceedingly rarely, if ever, visible at the optic disk. The

slow growth of the tumor would account for the absence of the choked disk, time being sufficient to allow of the formation of lateral drainage or gradual distention of the sheath.

When the patient was first examined the obtunding of the nasal half of the light field, together with the defective perception of green, pointed to interference with the conduction of the remaining active portion of this nerve. There was a concentric and a fairly equal contraction of the field for white and colors, pointing to a slow growth.

Professor Adami, who performed the post-mortem examination, found a large cancerous tumor of the pituitary. The bone in the neighborhood was found greatly atrophied and the fossa greatly enlarged.

The growth was not perfectly symmetrical, it extended more to the left than to the right-hand side. The right olfactory was pushed to one side, while the growth infiltrated anteriorly above the left olfactory nerve. The thyroid gland was found to be normal. There was no hypertrophy of any of the bones.

The portion of the tumor examined was inclosed in a laminated fibrous tissue capsule—the pia mater. The tumor was composed of rounded or oval masses of cells surrounded by loose connective tissue, the whole at first sight suggesting carcinoma simplex. On examining more closely, however, it was seen that the cells did not conform to the carcinoma type. The walls of connective tissue which inclosed the cellular masses were lined with elongated and flattened cells, fusiform when viewed edgeways. At other places, when the section was more oblique, these cells could be seen to be irregularly diamond-shaped, with large, clear, oval nuclei—typical endothelial cells. The cells forming the cell-masses were various in shape, being generally elongated with bluntly oval nuclei, others, however, being irregular in outline with a more rounded nucleus. They had in places a curious tendency to form small whorls, and in such cases the component cells were considerably flattened. The tumor was not specially vascular, nor did it show any tendency to degeneration. No pituitary structure was seen.

Diagnosis. Endothelioma.

The general symptoms of an intracranial growth, as headache, vomiting, vertigo, optic atrophy, were sufficiently pronounced to allow this diagnosis; and the locality of the growth was clearly indicated by the temporal hemianopsia.

An especial interest arises in connection with an explanation of the myxœdema-like state and the pallor of the skin. How are these conditions to be explained? Have they any connection with the destruction of the pituitary body?

In a recent paper by Pechkranz, of Warsaw (*Neurolog. Centblt.*, vol. xviii, p. 254), on a case of sarcoma of the pituitary body, par-

ticular mention is made of a myxœdematous-like appearance that was a prominent feature. The author considers it identical with the pachyacria mollis of Arnold, a state in which the dystrophy is confined to the soft tissues in contradistinction to acromegaly, to which he applies the term pachyacria ossea. In Pechkranz's case the osseous tissues were found normal.

In a few cases of myxœdema changes have been met with in the pituitary body, and instances are on record where both diseases have existed together. Dr. Anders (*Nervous and Mental Diseases*, January, 1892) reports a case of hemorrhagic tumor of the pituitary body and infundibulum in a case of pernicious anæmia in a female, aged thirty-four years. The symptoms which developed after typhoid fever were giddiness, headache, nausea, slight loss of consciousness, and delirium. I simply place this second case on record without the addition of any hypothesis as to a possible causal connection between the pituitary growth, the anæmia, and myxœdematous-like state.

DISCUSSION.

DR. STARR: I have been very much interested in this paper, because I had under observation a case that resembled quite closely the last one, in which the diagnosis of a tumor of the pituitary body seemed to be quite clear, on account of the general symptoms of brain tumor, the symptoms of blindness invading, first, one temporal field and then the other, and going on to complete blindness with optic atrophy. The patient saw Sir William Gowers, who concurred in the diagnosis, and the question of operation was submitted to Mr. Horsley, who decided against operating, and, I think, very wisely. I feel that while it is possible in some cases, on account of progressive hemianopsia, to make a diagnosis of tumor of the hypophysis, any one who has witnessed the operation of section of the fifth nerve within the skull will admit that operation upon such tumors is almost impossible.

CLINICAL TYPES OF THE URIC-ACID DIATHESIS.

By I. N. DANFORTH, A.M., M.D.,
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It does not require a very extensive or prolonged experience in clinical work to show a careful observer that the victims of the so-called uric-acid toxæmia present a considerable variety, as regards form, feature, complexion, temperament, and all other characteristics which go to make up the personality of the individual patient. In other words, there is no ideal or fixed type which brands the lithæmic patient, any more than there is an ideal or fixed type which marks the diabetic patient. But pretty careful study of my lithæmic patients for the past five or six years seems to show that nearly all cases will fall into one of three groups, although an occasional case may so nearly combine the peculiarities of two of these groups that it may be doubtful which one has the strongest claim. The typical cases, however, present no difficulties, and even the doubtful ones usually present the "ear marks" of one or other of the three groups if they are carefully observed.

As a preliminary, however, it is well for us to understand what we mean by a "lithæmic" patient, since the term can no longer be limited to those who have acid urine with a more or less copious deposit of uric acid or mixed urates. I would designate a person as a "lithæmic patient" whose urine is habitually strongly acid, high-colored, and of high specific gravity (1025 to 1030), now and then slightly albuminous, with mucin—*i. e.*, "cylindroid"—or occasional small hyaline casts, and which deposits uric acid or mixed urates, and perhaps oxalates on cooling. Such a patient is habitually "bilious," as the result of hepatic torpor, and the liver is frequently slightly swollen, the bowels are constipated, and the gastro-intestinal tract is distended with flatus, the tongue is coated, the breath is foul, and the

patient is constantly complaining of and dosing himself for "indigestion." Such cases include not only those in which uric acid is a visible and potential factor, but all cases which are the direct or remote consequence of the toxic effects of the alloxuric or xanthin compounds. Returning, now, to the postulate which forms the basis of and serves as the excuse for this paper, I repeat that in clinical experience we find three well-marked types of uric-acid diathesis, each type clearly and sharply defined by examples which are of frequent recurrence in hospital wards, dispensary *habitues* and office patients. These types I would classify as follows:

(*a*) The plethoric type.
(*b*) The neurotic type.
(*c*) The anæmic type.

In place of a detailed description of each type, I will illustrate by a brief description of cases, quoting from my office records.

(*a*) THE PLETHORIC TYPE. Examples of this type are very common in clinical experience. The patients are mostly middle-aged, "well-to-do" men in active business pursuits, frequently overworked and overburdened with financial cares, the so-called "hustlers," who make things come to pass, and without whose sturdy and often herculean labors most of the successful enterprises of this world would turn out failures. As illustrative of this type the following case is presented:

CASE I.—P. A. M., aged fifty years; weighs 194 pounds; is five feet ten inches in height; married; father of three healthy children; is a merchant, but a couple of years ago had a financial reverse, and has since filled a responsible salaried position in a bank. He first consulted me April 15, 1897. At this time he looked the picture of robust health, but physical examination showed slight cardiac hypertrophy, with a short, sharp, angry systole, and considerable arterial tension. The liver was perceptibly enlarged, and he had constant and annoying gastro-intestinal flatulence, with coated tongue, foul breath, constipation, and a whimsical appetite, although he was a rapid and rather a gross eater, "bolting" his food in a half-masticated condition. He had always been a temperate man, used no tobacco, and there was no history of venereal disease. He complained of some headache, occasional attacks of giddiness, a little shortness of breath after unusual exertion, backache, and occasional transitory or "flying" pains in the smaller joints of the extremities. Examination of the urine showed acid reaction, specific gravity 1015, urea 1.5 per cent., albumen a well-defined trace, no sugar, a copious deposit of lithic acid crystals, a few leucocytes, a few small hyaline casts and

numerous "cylindroids" or mucin casts. The quantity of urine varied from three to four pints in the twenty-four hours, so that the output of solids was practically normal.

Under appropriate treatment, a carefully regulated dietary, the free use of pure water, and an increase of out-door exercise, the albumen and casts disappeared, the lithic acid was reduced materially, and the troublesome symptoms gradually abated; in fact, he recovered in a technical sense, yet his peculiar constitutional tendency remained. He has still recurring lithic acid "showers," and every now and then requires "curing" over again.

What is the nature or what is the "diagnosis" of this case?

Not many years ago I would have made an off-hand diagnosis of "chronic interstitial nephritis," and a gloomy prognosis would follow as a matter of course. In a certain sense, it must be admitted, the diagnosis of "interstitial nephritis" would be correct, and yet it is a crude, superficial, and misleading diagnosis, because it is based upon a false and superficial view of the essential pathology; and as this case is presented as a type of a very common and numerous group, which in my judgment are frequently misunderstood, and are therefore subjected to maltreatment socially and therapeutically, I purpose devoting a few moments to the elucidation of what I believe to be the real nature or the intrinsic pathology of these cases.

First. There is present in all such cases a "catarrhal nephritis," as shown by the constant presence of slight albuminuria, few or more leucocytes, and the so-called "false casts" or "cylindroids."

Catarrhal nephritis, as a pathological entity, was described by me in detail in a paper read before the Illinois State Medical Society at its meeting in 1885, and, so far as I know, has not been described by any one else, either before or since that time. My paper fell still-born before the Illinois Medical Society, was quietly laid away in that "bourne" from whence no paper ever returns—the annual volume of *Transactions*, and has been sleeping there ever since. Nevertheless, the accumulated experience of the bygone years has assured me that a chronic catarrhal condition of the renal tubules—a condition analogous to catarrh of the bronchial tubes—is a common occurrence, is frequently associated with uric-acid toxæmia, and is undoubtedly, in most cases, caused thereby. It is quite possible for this simple catarrhal condition to remain uncomplicated and unmixed for long periods of time—weeks or even months—and then to recover, precisely as a bronchial catarrh may recover, without losing its identity

or changing its essential nature. *Therefore*, it is entitled to consideration as an independent pathological entity, and not merely as a symptom, or as a stage or stepping-stone to something else.

Secondly. There is also present in many cases belonging to this class an interstitial hyperplasia of the kidneys, in proof of which we find slight albuminuria, a few small twisted or distorted hyaline casts, and a certain degree of the cardio-vascular tension, long since described by Mahomed. It is not true, however, that "nephritis" is a proper term to apply to this process, inasmuch as it is not aggressively inflammatory in its nature, and does not result in renal hypertrophy followed by the small red kidneys, as is the case in true interstitial nephritis. It does produce a slow and sluggish nutritive hyperplasia of the embryonic connective tissue of the kidney, with induration of the organ, but without the wasting and distortion so characteristic of true interstitial nephritis. It is a very significant and interesting fact, that while this increase of connective tissue is going on in the kidney, precisely the same process is generally taking place in the liver, as Dr. Emil Boix has so clearly pointed out in his admirable little brochure on *The Liver of Dyspeptics*.

Thirdly. But while these palpable and visible lesions are undeniably present, they are not by any means the primary pathological factors in the cases under consideration; there is another factor which antedates the anatomical lesion by a long period of time—months or even years; and this factor is the constant presence of lithic acid or other unnamed and, perhaps, unrecognized compounds of the xanthin series. These bodies exert a peculiarly irritating or exasperating influence upon the connective tissues of both the kidneys and liver; sometimes manifesting their effect chiefly and primarily upon the kidneys, sometimes chiefly and primarily on the liver. In the majority of cases, I think, the kidneys suffer first and perhaps most; but in a respectable minority, certainly, the liver responds more promptly than the kidneys, and keeps in advance of these organs in the series of retrograde changes which follow. In all cases, both kidneys and liver become more or less involved, the difference being one of degree, and not of kind. If we seek to explain the occult influence which the lithic acid series wields over the connective tissues of the organs under consideration, we are at once confronted with insurmountable difficulties. Not until we have fathomed the mysteries

which surround the ultimate phenomena of normal nutrition; the conversion of normal pabulum into substance like itself by the normal cell-nucleus and the conversion of the nucleus itself into perfect and normal tissue, can we expect to explain the equally occult phenomena of abnormal or pathological nutrition. This, however, is true; that the presence of lithic acid and its allies in abnormal amount in the blood, especially if this condition is at all frequent, excessive, or permanent, is certain to set up in the connective tissue of the kidneys and liver a process of nutritive hyperplasia which results in a mild or partial cirrhosis of those organs.

What this mysterious influence is, how it is excited, why it selects the connective tissues instead of other tissues equally exposed to contact therewith, are, at present, questions which we cannot answer. We frequently call it "irritation," and its consequences "irritative hyperplasia," but such futile attempts at "explanation" are not quite in keeping with the present demands of medical science. Let us hope that the busy workers in our physiological and pathological laboratories will before long penetrate the mysteries which now surround the phenomena of normal and pathological cell-life.

It is important to sharply distinguish this form of cirrhosis from alcoholic cirrhosis, from which it differs both as to cause and effect—as to cause, in that it is not alcoholic, but lithæmic; as to effect, in that it does not destroy the organ involved, by progressive and irresistible cirrhosis, but is content with inducing a well-marked hypertrophy with some degree of induration, which, however, does not destroy the functional power of the organs, although it does abridge their vital capacity. Of course, in this category, I only include cases from which alcohol can be absolutely excluded as an etiological factor.

(*b*) THE NEUROTIC TYPE. The contrast between typical examples of these two types is very sharp and well-marked. Very many of the so-called "nervous temperaments," "neurasthenics," and "nervous cranks," as well as most of the cases of "nervous dyspepsia," are in reality cases of the neurotic type of lithæmia. The cases are about equally divided between men and women, with, at least in my experience, a slight preponderance in favor of men. Such cases present the same coated tongue, foul breath, and constipated bowels as we find in the former type. Gastric irritation with flatulence and, fre-

quently, gastric dilatation are generally present. The following case is presented in illustration of the characteristics of nervous lithæmia:

CASE II.—M. P. R., April, 1898, lady, aged fifty-eight years; married; mother of two healthy adult but markedly nervous children. Had cystitis two or three years ago without any tangible cause; is morbidly susceptible to changes of temperature; has had a few slight attacks of rheumatism years ago; looks healthy and well nourished, but says her "nerves are all on a wire-edge." Urine produces scalding when it passes, and she wants to "urinate all the time." Urinating does not produce relief, and she "cannot stand, walk, or ride without great discomfort."

At my first examination the urine was rather scanty (daily quantity not given), cloudy, highly acid, specific gravity 1030, no albumen, urea 1.75 per cent. (Doremus ureometer). The cloudiness disappeared on applying gentle heat. After standing a few hours a very copious deposit of lithic acid and oxalate of lime fell down. The microscope showed nothing but a plentiful crop of bladder epithelium. The tongue was coated, the bowels constipated, and the digestive tract was distended with flatus. The patient was exceedingly "nervous," slept poorly, and was quite depressed and worried about herself, so much so, that her family had begun to fear that serious nervous or mental symptoms might follow, an opinion which had been somewhat encouraged by an exceedingly capable neurologist.

Under appropriate anti-lithic, hygienic, and dietetic treatment, coupled with some moral treatment, her symptoms all disappeared, and she resumed her place in society and in church with her wonted vigor and capability. Her symptoms will return again and again, to be relieved in the same way, if at all. If she is treated as a "neurasthenic," and the lithæmic factor is overlooked, her symptoms will *not* be relieved, but in addition to "nervousness," she will develop cardio-hepatico-renal lesions of the gravest nature. I ought to add that careful inquiry elicited nothing to indicate that any pelvic lesion or irritation, past or present, could be blamed for her trouble, but that her symptoms were exclusively due to lithic-acid toxæmia.

(*c*) THE ANÆMIC TYPE. This type is not quite so common as the other two, but it is by no means rare. The patients are mostly women who have been overworked mentally or physically, or both—frequently young mothers who have borne children rapidly and have been burdened with their care; or saleswomen who are required to stand all day in a constant state of tension and excitement; or ladies who are engaged in clerical work; or school-teachers who find their vocation irksome and exhausting. Of course, males as well as females may and do have anæmic lithæmia, since some of the same causes obtain among men; but my own observation demonstrates that female

patients are largely in the majority. What is meant by "anæmic lithæmia?" If a hundred people undertake to do more work than they are able, especially of a kind which makes exhausting demands upon the nervous system, they will all sooner or later "break down," and manifest symptoms which will lead to some kind of a diagnosis and some kind of treatment. They will all show signs of exhaustion and impaired vitality. Some will present manifest symptoms of brain-fag; others will show unmistakable indications of circulatory disturbance, such as tachycardia and hæmic murmurs.

Neither of the foregoing groups are likely to claim admission to the lithæmic class, but there remains a group of anæmics that is unmistakably and indisputably lithæmic—a group in which the lithæmic toxæmia undoubtedly antedated and determined the anæmia; a group in which the anæmia will resist therapeutic measures unless these measures are combined with or preceded by measures specifically addressed to the relief of lithæmia. In this group of cases slight albuminuria will be present, and a few casts, either hyaline or cylindroids, or both; also a few leucocytes, some renal epithelia, a copious deposit of "red pepper," grains of uric acid, and probably crystals of oxalate of lime. The urine will be scanty, intensely acid, of high specific gravity, and will probably cause some cystic irritation and "scalding" when it is voided. The patients will generally be pale, depressed, or misanthropic, and such cases sometimes develop into actual "melancholia," although it rarely becomes permanent. The tongue is coated, appetite poor or fitful, bowels constipated, and the patient is constantly troubled with gastric and enteric flatulence. The following case will serve as an illustration of the foregoing statements. I might add many more from my office records, but one is sufficient.

CASE III.—Mrs. C. consulted me April 8, 1898. She is rather tall, spare, blue-eyed and blue-veined, pale and delicate; almost ethereal in her dainty refinement, and has "anæmia" written all over her in capital letters. She is thirty five years old, weighs 106 pounds; is married and has three children. No serious illness except parturition, and her labors have been quite normal and uncomplicated both as regards delivery and convalescence. In fact, her life has been singularly free from wear and tear, from sickness or from any other cause; yet she has been subject for several years past to periodic headaches or "migraine"; has suffered constantly from flatulent dyspepsia and constipation; has had a fickle and whimsical appetite, occasional attacks of hemorrhoids, and all other adjuncts of bad digestion and imperfect assimi-

lation. The menstrual function has always been perfectly performed, save that the flow has been scanty and rather colorless. The urine is scanty, high-colored, and rather frequently voided, but without pain. It is highly acid, specific gravity 1027, contains a trace of albumen, no sugar, 1 per cent. of urea, and throws down a copious crop of lithic acid on standing.

The centrifuge throws down "cylindroid" or mucin casts, showing the "catarrhal kidney," according to my peculiar but well-grounded views of renal pathology. I did not count the blood-globules, but a hasty examination of some slides easily demonstrated a decidedly abnormal number of white corpuscles. It would seem at first glance that an off-hand diagnosis of anæmia, anæmia pure and simple, uncomplicated idiopathic anæmia, could be made in this case without any danger of going astray. And precisely this diagnosis *had* been made again and again, and persistent treatment, based upon this diagnosis, had been carried out to no purpose, save a temporary appearance of gain, which amounted to nothing. But when the administration of hæmogenetics is preceded—and preceded long enough—by the administration of antilithics; when the scavenger organs have been made to resume their duties, so that elimimination is effectually carried on; when the digestive system is brought into a condition which enables it to appropriate both food and tonics, then, and then only, can tonics be expected to produce satisfactory results. In other words, when a case of anæmia is of lithæmic type and origin, it is futile to treat the anæmia as the primary malady; the lithæmic factor must be recognized and disposed of before any hæmogenetic treatment will result in positive good. Perhaps there is no error more common among us than to overlook the lithæmic cause underlying certain cases of anæmia; perhaps no class of anæmics respond more promptly to appropriate treatment than those which are associated with lithæmia. It has often seemed to me that the system fairly bounded back to health and vigor as soon as it was relieved of the incubus of the lithæmic poison.

It seems scarcely necessary to say that a pathological condition showing such a diversity of types cannot be treated by any hard and fast or uniform method. In many instances we are quite too much the slaves of so-called "principles of treatment"; in too many instances we are apt to accept symptoms as "indications for treatment" with the helplessness of true disciples of Spencer; but in no instance

have we followed the "indicatio symptomatica" with such dog-like fealty as in the treatment of lithæmia. It has come to be the accepted law that lithæmic patients must be dosed with alkalies, drenched with water, flooded with milk, and forbidden to touch meats, no matter what the physical condition of the individual may be. But this is a very absurd practice, which is condemned alike by common sense, science, and experience. Perhaps the blame may be partly due to the fact that many physicians seem to think that the treatment of the uric-acid diathesis consists only in the elimination of uric acid, forgetting that a much more necessary thing is to abolish or lessen the production of uric acid. In the treatment of the uric-acid habit it is the "indicatio causalis" that demands most attention—that is, the attempt to discover and remedy the cause of this sluggish, or it may be aberrant, action of the scavenger organs.

It is not the purpose of this paper to treat at length or in detail of the therapeutics and dietetics of lithæmia, as I propose relating the results of my experience on a future occasion. But I may properly add that the plethoric type of the uric-acid diathesis requires the vigorous use of antilithics and cholagogues for a considerable time, and their employment in lessened doses, weeks or even months, together with a diminished and carefully selected diet, from which nitrogenous foods are mainly excluded.

In the neurotic type the pathological condition is largely, sometimes wholly, due to nervous tension, nervous exhaustion, or excess of nervous wear and tear, so that the nervous centres are incapable of carrying on the work of elimination in a proper and satisfactory manner. Hence lithæmia; hence, again, the added increment of nervous irritation due to lithæmia, until the nervous system is "jangled and out of tune," or, as one of my patients expressed it, is on a "wire edge."

Now, the stock treatment of lithæmia for such a case as this would be sheer nonsense, worse than useless. The primary and most imperative demand is the use of measures which will relieve the extreme nervous tension and place the nervous system in a state of rest. Many patients recover when they are sent to the country for a period of rest and enjoyment. Minute doses of the salts of caffeine are very useful, and neuro-tonics are required. But the main thing is to take off the patient's harness and let the worn and jaded nervous system

rest and recuperate, so that it can resume its legitimate duties in a normal manner.

The anæmic type is more difficult to manage. In this the lithæmia, like the anæmia, is chronic; in fact, is part and parcel of the anæmia. Yet it is necessary to restore, in some degree, the power of elimination before much progress can be made toward curing the anæmia. The use of antilithics in small doses, judiciously employed, must precede tonics, and I am much given to the use of the caffeine preparations in this group of cases. Iron is badly borne, but phosphatic salts and strychnine are very useful. Manganese sometimes serves an admirable purpose.

I regret that I cannot here and now take the necessary time to speak of the treatment of lithæmia exhaustively, but this paper has already long exceeded the limit wisely adopted by this Association as a necessary protection against undue prolixity.

ON THE DIPLOCOCCOID FORM OF THE COLON BACILLUS.

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In the course of a careful study of a long series of livers, both cirrhotic and otherwise, we have in the specimens examined, with scarce an exception, encountered larger or smaller numbers of minute bodies, and the more we have studied them the more assured we have become that these are bacterial in nature. Under the ordinary $\frac{1}{12}$ immersion lens, and by the usual methods of staining these may easily be overlooked, and if recognized they may easily be mistaken for minute pigment granules present in the liver cells. But by more intensive staining and by employing a good $\frac{1}{18}$ immersion lens their nature becomes more evident.

The methods we have employed with the greatest amount of success have been by staining with carbol-fuchsin (one-half the ordinary strength) and subsequent bleaching in the sunlight in our earlier observations, and of late, almost exclusively, carbol-thionin, made according to the formula in Muir and Ritchie's text-book, the sections being cleared by aniline oil. Stained by either of these methods the granules resolve themselves in the main into the fine diplococci, surrounded often by a fine halo, as to the nature of which we shall speak later. When these diplococci are present in any numbers there may also be isolated minute spherical and ovoid bodies of the same dimensions, and there may also be seen occasional strings of three or four coccus-like bodies.

We have recognized these in the livers of man, the cow, sheep, rabbit, and guinea-pig. At first, working with the cirrhotic livers

of cattle and man, one of us was inclined to regard these as peculiar to cirrhosis, but, as already announced,[1] fuller study having shown their existence in the apparently normal liver, they cannot be regarded as specific of any one disease, although it is possible that they are one factor in the production of certain forms of fibrosis. Under these conditions they tend to take on a relatively deep stain, but in the majority of cases they stain badly, have a characteristic brownish tinge and would seem to be dead.

From several cases of cirrhosis in which these were recognizable cultures gave either vigorous, or what we must now regard as attenuated, growths of a colon bacillus, while after intravenous inoculation of adult rabbits with forty-eight-hour broth growths of our stock culture of the colon bacillus, which is in every respect typical, the liver cells showed these minute diplococcus forms in enormous numbers.

We were, therefore, led to conclude that, while it might be that other bacillary forms may also show a diplococcus-like appearance in the tissues, we had adequate evidence that the colon bacillus can show this appearance, and during the last few months we have conducted a long series of observations bearing more especially upon this diplococcus-like modification of the bacillus. Our work is divisible into two portions:

I. On the production of a diplococcoid form of the colon bacillus outside the organism.

II. On the diplococcoid form of the bacillus within the tissues.

The former portion has been undertaken in part by Dr. Nicholson; the latter portion and the studies upon growths in body fluids by Dr. Maude E. Abbott.*

Part I.

ON THE PRODUCTION OUTSIDE THE BODY OF A DIPLOCOCCOID FORM OF THE COLON BACILLUS.

While, under ordinary conditions of growth outside the body and ordinary staining by Loeffler's blue, for example, the colon is an

* But for the fact that, by my previous publication on the subject, I have made myself peculiarly responsible for these observations upon the colon bacillus, I would very gladly have left my own name off the title-page, for, in consequence of prolonged absence from my laboratories, the observations have been throughout conducted by Dr. Abbott, and Mr., now Dr. Nicholson, and I cannot sufficiently acknowledge the enthusiasm which they have thrown into the work.—J. G. A.

undoubted bacillus with no recognizable internal organization, it has been a matter of frequent observation that it might present distinct polar staining, and, indeed, when stained by fuchsin or other strong reagent for purposes of photography this so-called polar staining is very conspicuous. We need but refer to the various published photographs to confirm this statement. In these photographic reproductions of film preparations from cultures the majority of the bacilli are seen to be present as two rounded coccus-like bodies lying in close apposition, a common enclosing or joining sheath being more or less clearly evident.

The appearance here observed is that which is generally spoken of as "polar staining." It is common to a large number of bacteria, and, in not a few cases, as, for example, among the bacteria of hæmorrhagic septicæmia, has led in the past to not a little confusion in descriptions, authorities having been divided as to whether to class bacteria exhibiting the property in a marked degree as bacilli or diplococci. In certain cases, as in connection with the typhoid bacillus, it has been attributed to a retraction of the protoplasm to the poles during the process of preparation and staining of the film of bacteria, and thus has been regarded as an artefact.

We shall not here enter into the discussion concerning polar and metachromatic granules, but simply state that our observations, so far as they go, would seem to negative this latter supposition and to render it evident that, in the case of the colon bacillus at least, *there is a structural condition or internal organization of the microbe underlying and explaining such polar staining.* What is more, they show us that the appearances seen in the colon bacillus are closely allied to the "beading" to be made out in the tubercle bacillus under certain conditions of growth and environment.

As already pointed out by A. Schmidt,[2] Rodet,[3] and others, the colon bacillus varies according to the length of time it is kept outside the body, according to the medium in which it is grown, the reaction of the medium, the temperature, and the part from which it has been isolated. Rodet has found that when it is taken from the healthy intestine the individuals during the earlier generations outside the body are singularly even in their length and thickness and stain well throughout; when taken from diseased tissues, from the inflamed gall-bladder, for example, this is no longer the case; they are irregu-

lar, both in length and thickness; they stain irregularly, and show clear spaces and deeper staining portions.

He points out that a temperature of 44° to 45° leads, during the first few hours, to the appearance of very long filaments, though other individual forms are of the normal length. All these filaments show refractive bodies which take up intensely the basic aniline color. After twenty-four hours these long filaments disappear. In addition, according to this author, growth upon broth containing 2.5 per cent. lactose leads to the peculiar short and small forms, almost like cocci, the majority of which are double and in the form of diplococci.

These observations of Rodet have just come into our hands, and we can in the main confirm them. Indeed, in ignorance of this work, published two years ago, we have been working very much along the same lines as those indicated by Rodet, who, however, it may be added, has noted these appearances without studying more fully their nature.

We find that the long filaments mentioned by Rodet are to be observed in cultures kept for a few hours at a high temperature. It must not, however, be thought that they are exclusively confined to this period. Similar long filaments, showing even more clearly the presence of deeper staining bodies within them, are to be gained from old cultures associated with involution forms. Thus, in a specimen of our stock colon bacillus grown for a fortnight in broth containing a trace of bile we found great numbers of these long bodies, and associated with them numerous small diplococcoid forms. Perhaps the most interesting of these long filaments were observed in an agar plate culture obtained from the liver in a case of cirrhosis, which had been subjected for a few hours to a temperature of about 45° or 46°; removed from the incubator, this had grown, under difficulties (brought about by the partial drying-up of the medium), for four days at the ordinary temperature. In this the disposition of the deeper staining points was remarkable. (*Vide* Fig. 8, Plate I.) Seen under the $\frac{1}{18}$ immersion lens, after staining by carbol-fuchsin and decolorizing by weak acetic acid, these fine deeper staining points were arranged in a succession of pairs with occasional larger single ovoid bodies interposed. We have come across one other specimen of a rather prolonged growth, in which the same appearance was recognizable, though not quite so clearly. Possibly the exact extent of the staining and subsequent decolorization may have something to do with the diffi-

culty in recognizing this particular arrangement of the contained bodies.

We have also found that taking saliva, filtering and sterilizing it, and making cultures in this medium at the ordinary temperature, we obtain the production of these long filaments, which may be present in the growth not only during the first twenty-four hours, but during the continuance of the culture.

Under these conditions in the saliva of one of us (F. J. N.) the bacilli were throughout singularly slim, and in the later growths again they tended to show the development within the bodies of the bacilli of a succession of deeply-staining dots.

A. Schmidt has noted that he obtained these filamentous forms of the colon bacillus by the addition of caustic soda to broth. We found that we obtained the longest forms by employing lactose broth rendered 1.5° acid to phenolphthallein and containing 2.5 per cent. lactose. Here, more especially on the surface exposed to the air, at the end of twenty-four hours, we obtained remarkably long filaments. Indeed, we cannot agree with Rodet that the addition of this relatively large percentage of lactose to broth results in the production of the diplococcus forms. It is a misfortune that Rodet did not state more precisely the composition and the reaction of his broth.

In order to obtain the diplococcus form of the bacillus we conducted a series of experiments upon growth in broth of varying degrees of alkalinity and acidity at a temperature of 46°. Under these conditions it seemed certain that after the first twenty-four hours we obtained, more especially in slightly acid broths, a relatively increased proportion of short forms with polar staining, but we could not convert all the bacilli into the diplococcoid form. It was when we attempted to grow the bacillus upon certain of the body fluids that we met with the greatest amount of success.

The frequency with which we had encountered this diplococcus form in our observations on the liver made us wonder whether our method of gaining cultures might not have been, in part at least, accountable for the phenomenon. As Livingood[4] has shown, growth of the colon bacillus in organic juices expressed from the liver, spleen, etc., has some slight effect upon the morphology of this microbe. He noted that while the colon bacillus, in general, was relatively very large when grown upon *heated* liver juice, upon *unheated* he obtained very short,

thick, almost oval forms with abrupt ends, these occurring occasionally in pairs. Here in the development of these oval forms there is, it may be urged, an approach toward our diplococcoid form, but so careful an observer would have made a fuller note upon the subject had he recognized constantly the development of the diplococcoid appearance.

But it must be pointed out that there is a difference between inoculating a medium with a loopful of a culture—*i. e.*, with hundreds of thousands of a micro-organism, and employment of a medium in which what bacilli are present have gained an entrance through the ducts and excretory channels of the organs from which the fluid has been obtained. Working with bile, for example, we have frequently found that by making ordinary streak cultures in the usual method we obtained no results, whereas gaining the bile direct from the bladder by means of a pipette and adding a drop or two of this to broth, growths were obtainable.

The conclusion which we have reached is that in such cases the bacteria have been present in relatively small numbers, numbers so small that the somewhat weak inhibitory action of the bile has been sufficient to prevent growth when this bile has not been diluted. All our work goes to show, in fact, that bile has a slight inhibitory effect, not necessarily destroying the micro-organisms, but permitting growth to continue under unfavorable conditions, and it is under these unfavorable conditions that we have obtained either absence of growth or development of the diplococcoid form. For example, we have noticed in several cases that whereas with bile taken immediately from the body we have obtained no cultures, when a pipette of that bile has been kept for several days in the incubator, fairly numerous fine colonies of the bacillus coli have developed, in which the individuals show a tendency to assume the diplococcus form. These observations prepared us to find that the diplococcoid form of the bacillus might be a modification brought about by the action of the body fluids; but more especially were we led to employ these body fluids by two interesting observations.

In September, 1898, our attention was called by Dr. W. F. Hamilton to a case of what was diagnosed as atrophic cirrhosis in the medical wards of the Royal Victoria Hospital; this diagnosis was subsequently fully confirmed at autopsy. Through the kindly inter-

est of Dr. Hamilton we were present at the first tapping of the patient, and then obtained under careful antiseptic precautions sterilized flasks of ascitic fluid; at the same time a guinea-pig was inoculated with 10 c.c. of the same fluid, and cultures were made directly upon broth, agar, and blood-serum.

A full account of this case is on the point of publication by one of us, and we will here only give a brief epitome of the results.

Upon agar and Loeffler's blood-serum there developed scattered small colonies of a form which at first was taken to be a diplococcus, but which later, in the course of forty-eight hours, upon these media, as in the broth, showed the presence of definite stumpy bacilli, often arranged as short diplo-bacilli—in fact, the form which we recognize as very characteristic of the colon bacillus. Unfortunately, vacation time came on and the opportunity to fully examine these forms passed by. However, the guinea-pig died in twenty-four days, the autopsy was performed a few minutes after death, and from all the organs we obtained a pure culture of the colon bacillus, which appeared to be quite typical. Among the organs from which cultures were made was the gall-bladder; this gave a pure culture of the colon bacillus.

A pipette full of the bile of this guinea-pig, which possessed the characters dwelt upon by Welch and Blachstein[5]—*i. e.*, was clear, abundant, and of a relatively light color—showed, even when placed in the incubator, no apparent growth, but remained unclouded; at most, a few fine, granular flocculi were present after some days. But upon examining a film of this bile which had thus been kept, it was found to contain abundant minute diplococci. (*Vide* Fig. 12, Plate I.) These grew easily when transferred to agar, the colonies being minute and much smaller than those of the typical colon bacillus.

In the first transfer upon broth coccus and diplococcoid forms predominated, with occasional homogeneous stumpy bacilli. (*Vide* Fig. 1, Plate I.) Later transfers upon agar from this broth led to the development of the typical bacillary form—stumpy bacilli with rounded ends, often arranged as short diplo-bacilli, and showing a tendency toward polar staining. The morphological features of the cultures now became coarser, and resembled those of the ordinary colon bacillus.

Evidently, therefore, the bile of the guinea-pig exercised an inhibitory effect upon the growth of the colon bacillus, and this in two

directions. In the first place, the growth was peculiarly slow, so that the bile did not become turbid; in the second, the individual bacilli were distinctly modified—they were very much smaller than normal, and stained in such a way that they might easily be mistaken for minute diplococci. In fact, the resemblance between these minute diplococci and the minute diplococcus forms seen both in the cirrhotic and the normal liver is most striking.

What is true of the bile would seem equally true of the ascitic fluid taken from this case of cirrhosis. The fluid obtained was slightly opalescent, and upon keeping there gradually separated out a thin gelatinous proteid precipitate. Placed in the incubator, the fluid remained clear, and for the first few days appeared to be sterile; by the end of a fortnight, however, a granular deposit was distinguished, and now examination of the fluid showed the presence in it of singularly minute diplococci tending to be arranged in chains. (*Vide* Fig. 2, Plate I.) It may be remarked that this chain-like arrangement of the colon bacillus has been previously observed by Dunbar,[6] A. Schmidt,[2] and other workers.

Between the 3d of September and the 13th of October no less than five tappings were made, of which the third and fifth were subjected to examination. Both of these gave cultures upon broth and agar, showing diplococci merging into stumpy ovoid forms. Here, again, cultures when made immediately from the ascitic fluid showed forms of the colon bacillus, but the ascitic fluid kept in the incubator presented only pure cultures of an extremely minute diplococcus. After keeping for three weeks, subcultures upon agar made from the ascitic fluid no longer gave the typical colon form; instead of this a modified form was obtained; the individuals remained relatively small and very short. (*Vide* Fig. 5, Plate I.) Only after prolonged subculture and successive inoculation from 1 per cent. glucose broth did the forms become slightly larger and develop into a stumpy diplobacillus smaller than the typical colon. What is more, they did not induce fermentation of glucose or dextrose broth or cause the indol reaction. It must be pointed out that by this process of successive cultivation through glucose broth the form which was a characteristic diplococcus had become converted into a small bacillus arranged as a diplo-bacillus, and this stained homogeneously.

Upon passage through three guinea-pigs (the guinea-pigs being

killed from twelve to twenty-four hours after intraperitoneal inoculation) and growth upon 2.5 per cent. lactose broth the form has become still larger and more typical, but we still fail to obtain gas production. (*Vide* Fig. 6, Plate I.)

Within the last few days we have again obtained this diplococcus form from the human body. The patient, under Dr. Garrow, in the surgical wards of the Royal Victoria Hospital, suffering from marked biliary crises, was operated upon, in the expectation of finding a condition of cholecystitis with gallstones. Upon opening the abdomen a small amount of fluid presented, and a platinum loop of this was smeared upon agar-agar—this remained sterile—and immediately about a drachm of the fluid was collected, under strict aseptic precautions, in a sterile flask and brought over to the pathological laboratory. Here this was added to about an equal quantity of sterilized broth and placed in the incubator.

Upon continuing the operation the gall-bladder and ducts were found pervious; there was, however, a condition of perihepatitis, with subacute peritonitis affecting the upper half at least of the abdominal cavity, and with this was associated some thickening of the great omentum.

Upon examining the above-mentioned broth culture after twenty-four hours, Dr. Brown, the resident surgeon, found that it contained a pure culture of minute diplococci, and immediately called our attention to it. In the features of this growth upon various media this form has so far been found to resemble the minute diplococci already mentioned as obtained from the case of cirrhosis, though the growth is slightly more active and free. Passage through guinea-pigs and lactose broth has resulted in the development of a form identical with that just mentioned. (*Vide* Fig. 7, Plate I.)

There is very slow development of turbidity in ordinary broth, rather more rapid in glucose broth, but absence of any sign of fermentation. The growths upon the surface of agar in both were at first singularly fine, so that they resembled closely those of the streptococcus pyogenes, though possibly more transparent than the latter. Upon potato the growth was invisible; upon blood-serum the colonies were also very fine, and were of an opaque white fading on to a yellow tinge. Upon gelatin there was slow growth without liquefaction, while litmus-milk was decolorized until it became almost perfectly

white; then slowly, in the course of the fifth day or so, a fine pink color was developed in the medium; the milk is coagulated at the end of a week. Growth upon broth was definite, but not abundant, and was associated with singularly little turbidity, a white somewhat stringy precipitate being slowly formed. In the fermentation tube the open limb became opalescent or moderately turbid in the course of forty-eight hours, the closed limb remained perfectly clear, and, in addition, in neither glucose nor in lactose broth was there any production of gas; further, there was and is no indol reaction, and if turbidity be present it is still singularly slight.

It is unnecessary here to describe all the methods that we have employed in order to cause these forms to revert to type. Briefly, we may say that we have obtained the greatest change by culture for twenty-four hours upon broth rendered 1.5° acid, according to the method recommended by the Committee of Bacteriologists, to which 2.5 per cent. of lactose has been added. In this medium, already at the end of twenty-four hours, there is abundant growth and well-developed turbidity, and the individual forms are relatively large and ovoid, frequently arranged as stumpy bacilli. (*Vide* Figs. 6 and 7, Plate I.)

When this form is inoculated into the guinea-pig intraperitoneally and cultures made from the peritoneal fluid at the end of nine hours, both upon agar and glucose broth, growth upon glucose broth in the fermentation tube is much more active than before inoculation; and, whereas, previous to inoculation, only the open end of the tube had been rendered opalescent, now there is turbidity throughout both tubes. As already stated, after passage through three guinea-pigs and growth on this medium the form produced is undistinguishable from the normal colon bacillus.

It is possible that this remarkable and somewhat persistent diplococcoid form, obtained both from the bile of the inoculated guinea-pig and from the ascitic and peritoneal fluids, has become attenuated during its stay in the body, and that in the case of the bile, for example, during the passage through the liver, the colon bacilli have been markedly modified. We have taken sterilized human bile and added to this a minute quantity of a stock culture of the colon bacillus, and have not been able to obtain in the bile the diplococcoid form alone, although it is true that diplococcoid forms have been relatively abundant.

Here it is interesting to note a point which we again find observed by Rodet—namely, that the human bile has a distinct inhibitory effect upon the multiplication of the colon bacillus. Bile to which a minute drop of a twenty-four-hour old culture had been added remained to all appearances perfectly clear, and apparently no growth had occurred during four days; but when a drop of this bile was added to about 10 c.cm. of slightly alkaline broth and placed in the incubator, that broth rapidly became turbid, and there was most abundant development of the bacilli. We are making further observations upon this modification of the bacillus by growth in bile. This, however, may be said at the present time, that possibly the existence of bacteria in the bile may easily be overlooked when the ordinary methods of culture upon solid media are employed, the concentrated bile inhibiting their growth.

One of us (M. E. A.) has already found that human bile (three cases), which was apparently sterile when streaked upon agar-agar, gave abundant cultures of the colon bacillus when a small drop was added to about 10 c.cm. of glucose broth.

CONCLUSIONS. Thus far, then, our observations upon the colon bacillus grown outside the body have led us to the following conclusions:

1. The short form of the normal colon bacillus cultivated upon the ordinary bacteriological media frequently presents polar staining, the appearance given being that of two rounded bodies, staining more deeply than the rest of the bacillus, lying in and united by less deeply staining material.

2. In the more filamentous form a succession of these more deeply staining bodies is at times to be recognized.

3. Growth outside the body under relatively unfavorable conditions renders the polar staining more prominent, so that the shorter forms may closely resemble diplococci, and the filamentous forms show a common unstained or lightly-staining sheath, in which is to be made out a succession of minute dots in pairs and of somewhat larger single ovoid dots.

4. We have so far been unable by modifying the reactions of ordinary media, and by continued growth at a high temperature (46°), to produce cultures in which the diplococcoid form alone has been present, although by these means we have gained cultures in which this form has predominated.

5. On the other hand, certain body fluids sown naturally, if we may so term it, with the colon bacillus—*i. e.*, the ascitic and peritoneal fluids from a case of hepatic cirrhosis and of peritonitis respectively, and the bile of a guinea-pig inoculated with (? an attenuated form of) the colon bacillus have yielded us diplococcoid growths so modified that we have not so far been able to cause them to revert completely to type.

6. It has been by the prolonged action of these fluids that these races of the colon bacillus have been produced; cultures made from them immediately after removal from the body have yielded us, either immediately or after one or two transfers, typical cultures of the colon bacillus. Where the fluid has been kept from ten to twenty days the modified diplococcoid form has been produced.

7. The slight but definite inhibitory action of bile upon the growth of the colon bacillus is shown in two ways: (*a*) Smear cultures of bile upon agar may remain sterile, whereas the same bile added to ordinary peptone broth may be the seat of active growth. (*b*) Similar bile kept for several days in the incubator remains clear and shows singularly little evidence of growth within it, though subcultures from this yield fairly numerous colonies of a modified diplococcoid form of the bacillus.

8. The ascitic fluid from a case of hepatic cirrhosis was found to possess similar properties of modifying the colon bacillus and inhibiting its growth.

9. These modified colon bacilli are relatively minute, assume a diplococcoid form, are non-motile, form pin-point colonies upon agar-agar, cause but slight turbidity in broth and an almost invisible growth upon potato; act but slowly upon litmus-milk, have lost the power of fermenting glucose, lactose, and dextrose broth, and do not develop the indol reaction.

Part II.

ON THE DIPLOCOCCUS-LIKE MODIFICATION OF THE COLON BACILLUS IN THE TISSUES.

Taking a series of four young rabbits weighing from 225 to 305 grammes, we inoculated into the marginal vein of each 0.75 c.cm. of a twenty-four-hour growth of the colon bacillus, and killed the animals

at intervals of fifteen minutes, thirty minutes, one and two hours. The various organs were immediately placed in formol-Müller, and were subsequently cut in celloidin and paraffin, the sections being stained by carbol thionin.

Our attention was at first especially directed to the liver. Here already in the animal killed at fifteen minutes after intravenous inoculation a definite series of changes was seen to have occurred. (*Vide* Figs. 13 and 14, Plate II.) In the bloodvessels of the liver free bacilli of normal size and appearance were occasionally to be observed, but already bacilli could be recognized within the leucocytes in the blood-stream. (*Vide* Fig. 13.) The number of these leucocytes was not excessive, but each contained a relatively large number of bacilli. In addition, already the endothelium lining the vessels was seen to be very prominent; here and there these cells contained a fairly large number of bacilli.

In thirty minutes the number of bacilli in the endothelium cells and the number of endothelial cells containing bacilli were markedly increased. The bacilli, situated within the endothelial cells, already show strongly marked differences from those free in the blood-stream. The latter were of normal length and thickness, and took on a homogeneous stain. Those within the endothelial cells were short and stumpy, sometimes almost coccus-like. The appearance given is that of primitive bacilli having been broken up into shorter lengths.

In the rabbit killed at the end of one hour the number of bacilli seen in the blood-stream was distinctly less, but there was a further increase of those in the endothelial cells. Occasionally, in the endothelial cells relatively large bacilli could be seen, but the majority of forms were, as in previous specimens, very short and stumpy, and the impression gained by a study of the sections is that the bacillus is taken up in the long form and subsequently broken up into shorter sections. So far no well-stained bacilli could be seen in the liver cells. Already in the endothelial cells certain of these stumpy forms had the appearance of diplococci of fair size.

In the liver of the rabbit killed at two hours after inoculation the same appearances were to be made out as those seen in the rabbit of one hour—namely, the presence of short and stumpy bacilli in the endothelial cells; we were of the opinion that a larger proportion of these had the appearance of diplococci than in the previous sections.

In several places between the liver cells, as indeed also in sections taken at an earlier period, there were to be made out hyaline masses, apparently situated within the vessels, which hyaline masses contained numerous bacilli. We have found some little difficulty in coming to a conclusion as to the nature of these masses; the large ones would seem certainly to be hyaline thrombi, but in the smaller ones it was often difficult to make quite certain whether we were not dealing with some phenomenon in connection with the endothelial cells; for very frequently a nucleus of endothelial type was in close connection with these smaller hyaline masses. We could not absolutely leave out of account the possibility that we were dealing with very greatly swollen endothelial cells.

Up to this point we were unable to recognize in any of the sections of this series indications that the bacilli had been taken up by the liver cells. But in a rabbit killed four hours after inoculation we came across great numbers of extremely minute brownish shadows definitely within the hepatic parenchyma. (*Vide* Fig. 15.) We have been wholly unable to stain these little bodies, and, indeed, only by very careful examination with the $\frac{1}{18}$ immersion lens have we been able to see them distinctly; but with this magnification there they most certainly are, and the more carefully they are studied the more clearly they are seen to be present in general as extraordinary minute little brownish diplococci, at times showing a halo around them. And the more one has studied these appearances the more it seems likely that this apparent halo indicates that these small bodies lie in vacuoles, although in part also the appearance may be due to the existence of an unstained sheath or body-substance.

Evidently, judging by the sections from this stage of the inoculation disease, not only are the bacilli taken up in large numbers into the liver cells, but being taken up they undergo rapid digestion and destruction, so that they can no longer be stained by the ordinary methods, and what we see are essentially the shadows of the bacilli. We have attempted to make out the stages by which the bacilli pass from the endothelium into the liver cells, but so far without great success. Here and there in sections of the two-hour rabbit we have been able to make out that the endothelium appeared to be raised from the underlying cells, and on the inner side of this endothelium very rarely we could see in the spaces between the endothelium and

cell well-stained coccus or diplococcus-like bodies. We are, however, unwilling to dwell too strongly upon these appearances, inasmuch as the endothelial cells showing these features were crowded with bacteria, and we could not exclude the possibility that in the process of preparation the cells might have become slightly dislodged, and that the appearance of the bacilli apparently outside the main body of the cells might be due to their presence in a slightly different plane.

Taking next well-developed rabbits similarly inoculated and killed at the end of twenty-four hours, we have found in them the presence of bacilli in the endothelial cells, while the brown shadows, as we may term them, have been present in enormous numbers in the liver cells.

Thus far, then, from what we have said, it would appear evident that when the colon bacillus enters into the circulation it is liable to be taken up rapidly by the endothelium lining the hepatic vessels, and in this process undergoes division into smaller segments, so that in the main one meets with stumpy forms in these cells, forms which still stain well, although often showing a tendency toward a diplococcoid appearance. Following up this within four hours these bacilli are discharged by the endothelial cells, and are by some means or other taken up by the hepatic cells and rapidly destroyed, so that it is only by careful examination that minute coccus or diplococcus-like bodies are discovered within the liver cells.

It is interesting to note that upon examining a film of the bile taken from inoculated animals at the end of twenty-four hours one can by careful preparation recognize in it these very minute diplococcus-like bodies. To see them it is necessary to make a very fine film, treat with weak acetic acid, wash, and then stain with dilute carbol-fuchsin, and examine under the highest power. It would, therefore, seem evident that the liver cells are capable of discharging these modified and destroyed bacilli into the bile capillaries.

But we now come to certain great difficulties in connection with the statements here made. In the first place, making a large series of control observations upon the livers of apparently normal adult rabbits we have frequently come across these same diplococcus-like bodies, and in four instances in relatively very great numbers. Indeed, these diplococcus-like bodies would seem to be very frequently present, more often present than absent from the rabbit's liver.

To obviate this difficulty, it seemed to us that we might obtain more decisive results by employing very young rabbits from three to six weeks old. In our control sections of the livers of these very young rabbits we have found that the diplococci appear to be absent. Upon making a like series of inoculations into these very young rabbits, and killing at two, four, and twenty-four hours, we hoped definitely to settle the question. But here, at first, we had wholly negative results. By our routine methods of staining we were unable to detect any bacteria within the cells, even when we employed sections that had been cut in paraffin. So opposed to all our previous results and conclusions did these appear that for a time we were on the point of relinquishing this paper. It is possible that either the carbol-thionin used by us for the experiments was defective or our technique modified in some slight degree, for at the best the carbol-thionin method does at times show itself wanting. But our failure was so constant that we hardly believed that this explanation would suffice.

Now we have attempted to stain other sections from the same blocks by other methods, and we eventually found that staining for half an hour with Loeffler's methylene-blue, washing with tepid water, and then passing through absolute alcohol and zylol, we obtained sections in which the tissue is relatively faintly stained and in which we are able to detect within the cells peculiar small diplococci having the faintest brown tinge. These were obtained from the livers of animals which had been inoculated two and four hours before death. Our failure to recognize these bodies is in fact due to their minute size and their very faint stain. We have examined control livers also from young animals by the same methods with negative results.

It would seem clear to us that the rate at which the colon bacilli are taken up and destroyed in the liver varies to some extent in different animals according to the condition of the tissues and the virulence of the microbe. It is to be noted that the culture employed in this latter series was from the same stock as that employed previously—a stock which had been grown outside the body for an additional six months. And here we may notice that the most powerful staining diplococci, and also those having the deepest brown tinge, were in the livers of rabbits dying from three to four weeks after inoculation, as again in certain of our control animals. Our experimental animals, which had been kept alive at the most for twenty-four hours, have

yielded us only diplococcus forms, showing but a delicate brown staining within the cells.

While we were in doubt with regard to this second series of livers, it seemed to us well to study another excretory organ not in connection with the portal circulation. Examining the kidneys of several control rabbits, we have in no case been able to find the diplococcus forms present within the organ in the great numbers in which we have come across them in the livers in the same animals. We have met with occasional diplococci within the cells of the convoluted tubules, but these have been rare. We have found that the examination of the kidneys for these modified colon bacilli has been a matter of considerable difficulty. Undoubtedly they are taken up by the cells of the convoluted tubules. Of this we have abundant evidence, and occasionally we have come across well-staining diplococcus-like forms in the outer portion of the kidney cells, but the diplococcus forms appear to be destroyed with great rapidity, and in the process of destruction do not assume the brownish tinge already referred to in connection with the liver; thus it has been a matter of extreme difficulty to trace them. We have, however, seen them in great numbers in the cells of the convoluted tubules of the rabbit two hours after inoculation (*vide* Fig. 11, Plate I.) and again at twenty-four hours, in this latter the number being greater. Here, also, in the cells of the tubules in very thin sections we have come across numerous minute vacuoles of an elongated oval shape, often slightly dented in the middle; and within these we have at times been able to distinguish two very minute dots, evidently the very final indication of the disappearing and destroyed bacillus. (*Vide* b. and c., Fig. 11.) Independently, Dr. A. G. Nicholls[7] has studied the kidneys of the animals inoculated by us and has met with these diplococcus forms, fully confirming what we here state.

CONCLUSIONS. Our observations, therefore, upon the whole would lead us to the following conclusions:

1. That the colon bacillus injected into the circulation is rapidly taken up both by the liver and the kidney.

2. That within fifteen minutes after inoculation some bacilli are already ingested by the endothelial cells in the liver, this process of ingestion continuing until these cells are full of bacilli.

3. That in this process of ingestion the bacilli are broken up into

shorter lengths, and that these short stumpy bacillary forms may—already within the endothelial cells—present themselves as two deeply staining dots, and may thus resemble diplococci.

4. That already in two hours the modified bacilli may be discharged outwardly from the endothelial cells and be taken up by the underlying liver cells.

5. The exact stages of this discharge we have been unable to follow. In the liver cells the modified bacilli are to be recognized as small diplococci of a size varying from that equal to the diplococci seen in the endothelial cells down to points of extreme tenuity. Evidently these forms are undergoing destruction.

In the first place, they lose their power of staining; in the second, if the destruction is not too rapid, they assume a brownish tinge. What is the causation of this brownish tinge we have not yet determined, but it is to be made out in the unstained sections, and our studies upon the human liver indicate to us that not a little of the fine pigmentation common in liver cells is brought about by the existence in these cells of these minute elements of bacterial destruction.

During this process of destruction the modified bacilli lie in digestive vacuoles, and the frequent appearance of the halo around these forms is in a great part due to the existence of the vacuole. We have occasionally been able to make out what appear to be these vacuoles in the liver cells without the evidence of the contained microbe, that having been apparently entirely digested. (We have seen the same appearance also in peritoneal leucocytes nine hours after intraperitoneal inoculation with modified colon bacilli.) (*Vide* Fig. 10, Plate I.)

6. In the kidney the same process is at work. We have recognized the diplococcus form within the cells at the expiration of two hours after inoculation, and have also seen the vacuoles within the cells and convoluted tubules, and there have occasionally met with two dots just visible, being final indications of the process of digestion of the bacillus.

We sincerely hope that others will repeat and confirm these observations, though to those repeating them we would point out that it is absolutely essential to employ higher powers than those ordinarily used for bacteriological investigations, while the finest sections are requisite to give clear results. Very careful technique in the matter

of intensive staining and of decolorizing of the tissues is also an essential. Unless these points are attended to our frequent difficulties in forging the chain of evidence here brought forward will certainly present themselves, and, without great patience, we cannot expect others forthwith to corroborate our results. We are prepared, that is, to find these results called in question; but after many months, and on the part of one of us many years, puzzling over these peculiar pigmented bodies, seen more especially in the liver, we do not see what other conclusion to reach. Here we may say that we are prepared to find bacteria other than the colon when taken up at the cells of the liver and kidney assume very similar forms. Indeed, we already have evidence of this in connection with the typhoid bacillus.

If the above conclusions are correct, it is clear—judging from what we have said concerning the appearances seen in many normal livers of rabbits, and seen also, we may add, in the human liver—that the liver as an organ possesses the most important function of taking up and destroying bacteria, more especially the colon bacilli, which have gained admission through the portal blood, while the kidney possesses a like power of rapidly destroying bacteria circulating in the general systemic blood.

As our paper is more especially upon this diplococcoid form of the colon bacillus and its modifications within the body, we will not here dwell upon this subject, especially as one of us has already called attention to this conclusion elsewhere.[1]

We purpose, if possible, making a series of observations upon those conditions which lead to the taking up of bacteria from the intestines and upon their course through the blood, and again through the lymphatic system.

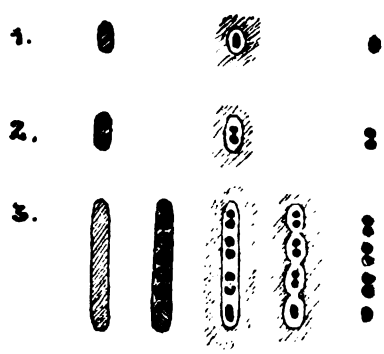
Finally, a few words regarding the structure of the colon bacillus to be deduced from the above observations. It is difficult to arrive at any other conclusion than that the type colon bacillus is a stumpy bacterium with rounded ends. This bacillus consists of at least two parts—one which takes deeply the stain, the other relatively non-staining. Under ordinary conditions of free and rapid growth these are not to be distinguished from each other; under other conditions, more especially those of difficult growth, the chromatin or staining portion tends to be aggregated along the long taxis of the bacillus, most characteristically in the stumpy bacillary form, as two rounded bodies,

and thus the appearance is given of a diplococcus, a capsulated diplococcus, the apparent capsule being the non-staining body-substance.

Where the bacillus is of the large or filamentous type our observations would seem to show us that the filament is capable of being broken up with a certain amount of ease—*e. g.*, in the endothelial cells—into its component stumpy or bacterial forms, each of these being either a single oval deeply staining body, or, as above mentioned, two rounded staining bodies, so that it assumes the diplococcus form. The size of these chromatin bodies varies, as would be the case were the chromatin capable of varying degrees of concentration.

Judging from what is observed within the hepatic and renal cells, these chromatin bodies consist, at least, of a basal non-staining material and a chromatin, for the power of staining (with aniline dyes) may completely disappear, and, nevertheless, a substance is left behind still capable of recognition as a minute diplococcus, unstained by ordinary reagents, but, within the liver cell, capable of assuming a brownish tint. From the appearance within the body cells this central substance is obviously more resistant than the remainder of the bacillus. It is the last part of the bacillus to be destroyed; indeed, these diplococcus-like shadows of bacilli may accumulate more especially within the liver cells, the mesenteric and retroperitoneal glands.

We will not here discuss the recent work upon the existence of nuclei or nuclear material in the schizomycetes. It is, however, impossible not to be struck by the analogy in structure between the colon bacillus as here described and nucleated cells in which nuclear division precedes cell division. For we have encountered the following forms:



This paper being already longer than we had intended to present, we have omitted any consideration or criticism of the observations by Gärtner,[8] Klein,[9] Thiercelin,[10] and many others which show a recognition or failure of recognition of the existence of this diplococcoid form of the colon bacillus, and very frequently a tendency to mistake the diplococcoid and the encapsulated form of the colon bacillus for an entirely different species. This subject will be discussed at greater length by one of us (M. E. A.) in a separate article.

Explanation of Plates.

The figures of bacteria have all been drawn (by J. G. A.) under the same magnification—*i. e.*, Reichert $^1/_{18}$ in. immersion, ocular 4—by means of a Zeiss camera lucida, latest pattern. All were subjected to the same process of staining: Ziehl-Neelsen carbol-fuchsin diluted with 50 per cent. of water. They were relatively deeply stained and then decolorized in water containing a minute proportion of acetic acid—about one drop of glacial acetic acid to the ounce of water. The drawings of sections were made under the same conditions, with the exception of Fig. 11, Plate I., which is a tracing from a photograph.

Plate I.

Fig. 1.—Growth originating from bile of guinea-pig which died twenty-four days after intraperitoneal inoculation with 10 c.cm. of ascitic fluid from case of hepatic cirrhosis; forty-eight hours' growth in alkaline peptone broth inoculated from forty-eight hours' culture upon agar-agar, which in its turn had been seeded from a pipette of the guinea-pig's bile removed a few minutes after death and kept for eighteen hours at 37°.

Fig. 2.—From film made from the ascitic fluid of the above case of hepatic cirrhosis left in sterilized flask at 37° for seventeen days.

Fig. 3—From first broth culture, forty-eight hours old, made from the above ascitic fluid. Note minute ovoids as well as diplococci.

Fig. 4.—From forty-eight-hour culture upon Loeffler's blood-serum made direct from the above ascitic fluid: forms a shade larger than those from broth, with slight tendency to be arranged in short chains.

Fig. 5.—The same micro-organism after repeated transfer upon agar-agar during six months: individuals much larger, although still relatively small, with short bacillary, diplo-bacillary, and diplococcoid forms.

Fig. 6.—The same after transfer through three guinea-pigs, followed by three successive transfers through 2.5 per cent. lactose broth: the bacillus now is morphologically indistinguishable from the forms seen in Fig. 1 and (save in absence of flagella) from the ordinary colon bacillus.

Fig. 7.—Microbe isolated from peritoneal exudate in case of peritonitis with perihepatitis after parallel passage through three guinea-pigs and transfer through lactose broth. The microbe, upon first isolation, was a minute diplococcus: it will be seen to be undistinguishable from that shown in Fig. 6; culturally, it was identical.

Fig. 8.—To show arrangement of diplococcoids and ovoids in filamentous form of a colon bacillus isolated from the spleen in a case of progressive hepatic cirrhosis. From a colony on an agar plate kept five days under unfavorable conditions (vide *British Medical Journal*, October 22, 1898).

Fig. 9.—From film made from the bile of a rabbit killed seven hours after intravenous inoculation with the colon bacillus; the bile was kept fourteen days in pipette before examination. Note variety of forms: rare short bacilli and diplo-bacilli with slight capsule, diplococci with well-marked capsules, minute diplococci devoid of capsule (? destroyed).

Fig. 10.—Cells from peritoneal fluid of guinea-pig killed nine hours after intraperitoneal inoculation with a forty-eight-hour broth culture of form shown in Fig. 5—*i. e.*, from agar cultures derived from the ascitic fluid from a case of cirrhosis. Stained with carbol-thionin,

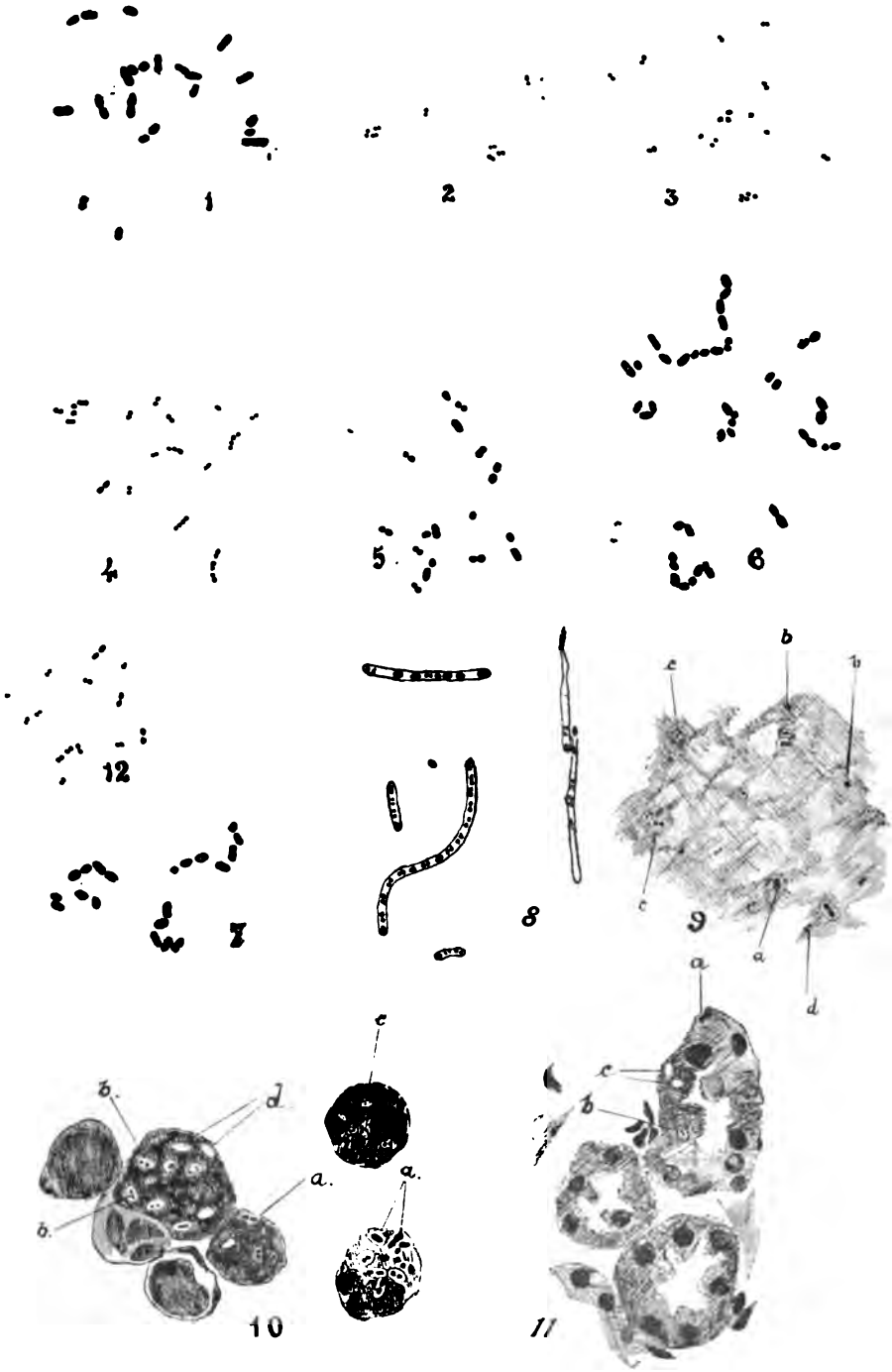


PLATE I

Adami—Diplococcoid Form of the Colon Bacillus.

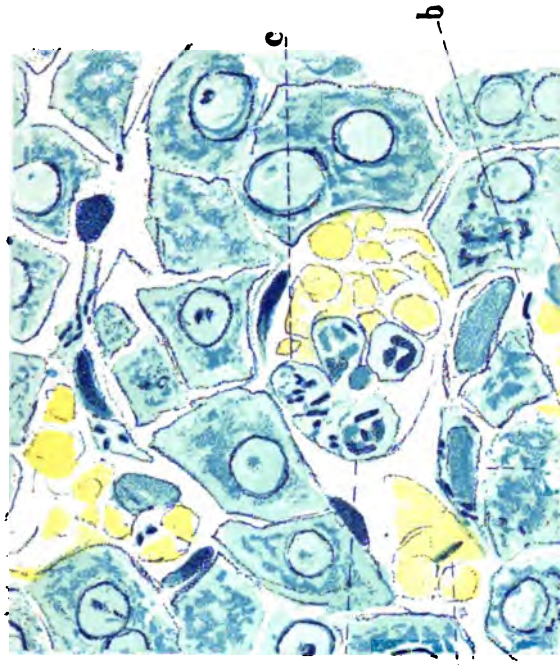


FIG. 13.

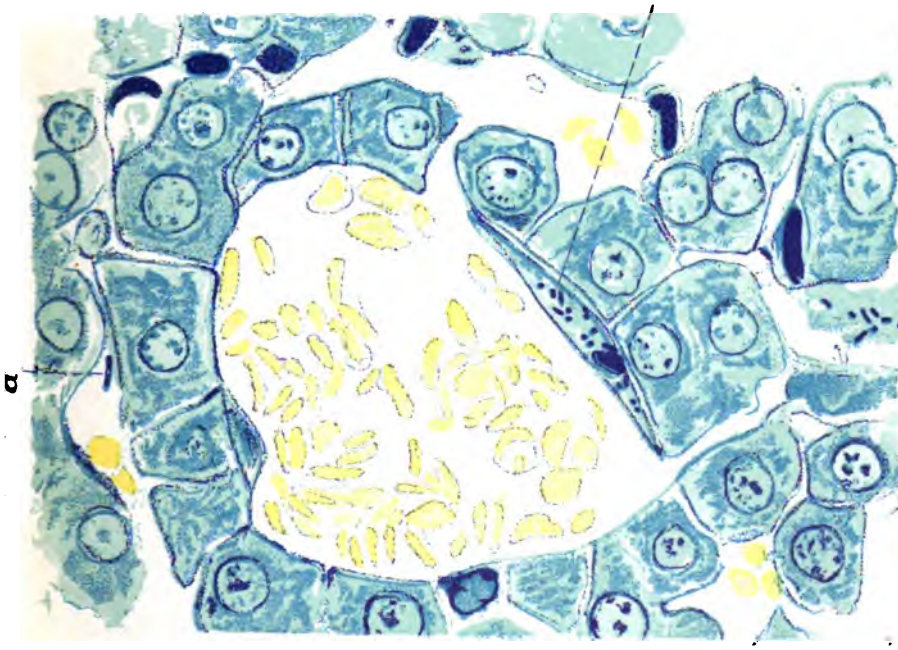


FIG. 14.

PLATE II

Adami—Diplococcoid Form of the Colon Bacillus.

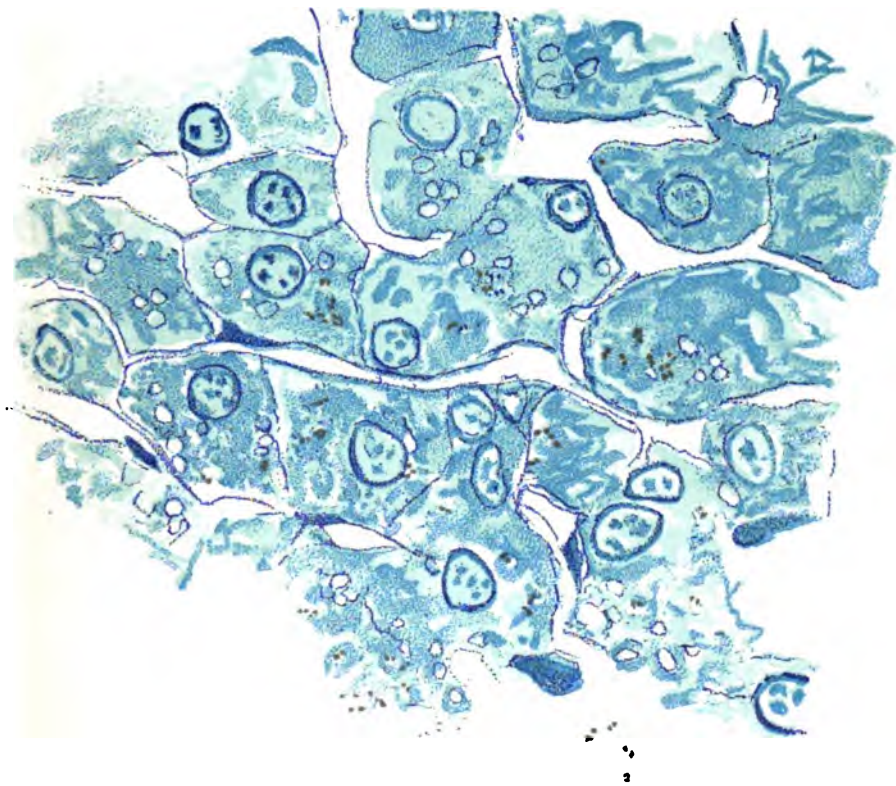


FIG. 15.

PLATE III

Adami—Diplococcoid Form of the Colon Bacillus.

Reichert $^1/_{18}$ in. immersion, ocular 4, drawn under a Zeiss camera lucida. *a*. Deeply staining bacterial and diplococcoid forms. *b*. Attenuated diplococcoids in large vacuoles. *c*. Still further attenuated diplococcoids. *d*. Vacuoles void of contents.

FIG. 11.—From section of convoluted tubules of kidney of young rabbit killed two hours after intravenous inoculation with pure culture of bacillus coli. Tracing from photograph under Zeiss $^1/_{18}$ in. immersion, compared with original section (the photograph not being perfect). *a*. Deeply staining diplococcoid form just within cell of tubule. *b*. Attenuated diplococcoid form in vacuole. *c*. Empty vacuoles of oval shape.

FIG. 12.—To compare with Fig. 1. From film of bile from guinea-pig kept in pipette and placed in incubator at 37° for eighteen hours. A drop of this same bile passed through broth and agar gave the form shown in Fig. 1. Note presence of ovoids, diplococcoids, and diplococci.

PLATE II.

FIG. 13.—Section of liver of rabbit killed fifteen minutes after intravenous inoculation with 0.5 c.c. of forty-eight-hour broth culture of B. coli; carbolic thionin; Zeiss camera lucida; $^1/_{18}$ oil immersion.

a. Marked swelling and enlargement of endothelial cell with ingestion of bacilli, which have become short and stumpy.

b. Free bacilli, remaining long.

c. Leucocytes containing bacilli.

FIG. 14.—Section of liver of rabbit killed fifteen minutes after intravenous inoculation with 0.5 c.c. of forty-eight-hour culture of B. coli; carbolic thionin; Zeiss camera lucida; $^1/_{18}$ oil immersion lens.

a. Bacillus free in capillary.

b. Endothelial cell, much swollen and containing several bacilli, both stumpy and tending to assume diplococcoid form.

PLATE III.

FIG. 15.—Section of liver of rabbit killed four hours after intravenous inoculation with 0.5 c.c. of forty-eight-hour culture of B. coli; carbolic thionin; Zeiss camera lucida; $^1/_{18}$ oil immersion lens.

Abundant very minute diplococcoid forms in liver cells, part of which only are shown.

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7. Nicholls. Philadelphia Monthly Medical Journal, January, 1899, No. 1, and Montreal Medical Journal, 1899, xxviii. p. 161.
8. Gärtner. Centralbl. f. Bakteriologie, 1894, xv. p. 1.
9. Klein. Ibid., p. 276.
10. Thierclein. Comptes rendus de la Soc. de Biologie, 1899, 10th series, vi. p. 269.

DISCUSSION.

DR. WELCH: Dr. Adami's observations are of great interest and most suggestive, although their interpretation is not without difficulties. The colon bacillus is undoubtedly encountered very often in bacteriological examinations at autopsies, but only in a relatively small number of these cases does its presence seem to be of any pathogenic significance. Blachstein's

experiments showed that colon bacilli injected into the circulation not infrequently cause necrotic foci in the liver, where they may survive a long time, and that the bacilli are often eliminated by the bile. We found weeks, and even months, after the injection the bacilli in the bile, in which they had induced certain changes suggestive of the causation of gallstone by biliary infections.

Dr. Adami and his coworkers have brought forward new observations in support of the opinion that bacteria are very frequently absorbed from the intestinal tract, and that certain organs, particularly the liver, dispose of these bacteria by intracellular digestion. Under the designation of the "diplococcus form" of the colon bacillus, Dr. Adami describes conditions and appearances of this bacillus, which I judge not to be identical, and it is possible that some better designation might be used. I confess to a feeling of some uncertainty as to the exact interpretation of the small coccoid bodies demonstrated by Dr. Adami in the hepatic and other cells, but I do not question that he has brought forward to-day and in his previous papers strong arguments in favor of his conclusion that they are bacterial forms or are derived from such forms.

DR. ADAMI: This subject opens up to a large field, and there is yet so much to be done, in order to establish the fundamental points in connection with the reaction of the tissue cells on the colon bacillus under normal and pathological conditions, that I fully accede to Dr. Welch's statement, that this matter must at the present time be received tentatively. I cannot expect others who have not worked at the subject to accept freely and immediately the observations which I have just recorded; indeed, the observations upon this very minute form require very great care. Thus I recognize that it may be some years yet before the statements here made receive general acceptance, and I am myself prepared to spend some years yet in working at the subject. I have, however, seen sufficient during my work this last year to feel assured that others must eventually see that my observations are fundamentally correct.

ON THE TOXICITY OF THE URINE.

By F. FORCHHEIMER, M.D.,

AND

R. W. STEWART, M.D.
OF CINCINNATI.

The question of the toxicity or non-toxicity of urine has been engaging the attention of scientists for a long time, and the number of authors who have contributed to this subject is very great. From a practical point of view the subject has received its greatest impetus by the appearance of Bouchard's charming book,[1] translated, with a preface, by Thomas Oliver.

Without going into a chemical discussion of the agents producing toxicity of urine, this work has offered to us a simple practical test, which consists in injecting a quantity of urine proportionate to the weight of the animal; if the animal dies, the urine is toxic; if not, there is no toxicity. Now, to those of us who believe in auto-infection as an important etiological factor in disease, this test was very welcome; first, because it appealed to us on account of its simplicity; and, secondly, because it seemed to give us an index as to the prime cause of the diseased condition of our patient. It could not be final or complete, because of the fact that the substances which produce toxicity in urine had not been isolated; and, therefore, their origin in the body not discerned. But under all circumstances, this test seemed a valuable one for clinical purposes; and, probably, more exact than many others upon which diagnoses are based.

As this paper has not been prepared as a literary digest of the subject, but simply to determine a method by which the toxicity of urine

[1] Leçons sur les Auto-intoxications dans les Maladies, etc. Paris, 1885; Philadelphia and London, 1894.

can be determined, and to discuss conclusions arising from the comparatively large number of experiments made, we will be justified in beginning with Bouchard.

Bouchard's method consists in injecting in the rabbit from 30 to 60 c.c. (average 45 c.c.) per kilo of animal into "the posterior marginal vein on the dorsal part of the face as it spreads over the ear." (Bouchard, *loc. cit.*) He discards subcutaneous injections, because, as he has proven by experiment, absorption does not take place with sufficient rapidity.

One of us[1] first began using a modification of Bouchard's methods by injecting the urine into the peritoneal cavity of rabbits under certain aseptic precautions, a method which was afterward fully justified by the investigations of Vollhard,[2] by whom is disclosed the fact that in intravenous injections the results are changed by the rapidity of the injection, by the pressure which is used, and, finally, that in two cases extensive thromboses were produced by urine injected intravenously. But that which finally induced us to discard the method of Bouchard and the subsequent observers, was the fact that there were so many differences of opinion expressed, especially in connection with the toxicity of urine in pregnancy, and that, with one of us, experiments made with the urine of one patient gave absoluely varying results.

The tentative conclusion was arrived at that it was not the observers that were at fault but the method. To prove or disprove this view, both of us began a series of experiments: the one taking the urine of pregnant women during the last month of pregnancy, and the other that of healthy subjects and of patients who could be considered from clinical manifestations, and are so considered by Bouchard, as being affected with gastro-intestinal auto-infection. Bouchard speaks of these cases as being primarily connected with dilatation of the stomach. We have failed to find the stomach dilated. These patients were:

CASE I. A young woman, aged thirty years, suffering with chronic constipation, headaches and hysterical (neurosal type, Bouchard).

CASE II. Female, aged forty-five years, constipation, Riggs' disease, headache, dyspepsia and recurrent urticaria.

[1] R. W. Stewart: Toxicity of Urine of Last Month of Pregnancy. The American Journal of Obstetrics and Diseases of Women and Children, xxxv. 3, 1897.

[2] Monatsschrift für Geburtshülfe u. Gynäkologie, Studien zur Pathogenese d. Eklampsie, 1897.

CASE III. Male, aged fifty years, constipation, dyspepsia, asthma (asthmatic form, Bouchard).

CASE IV. Female, aged thirty years, constipation, migraine (neurosal form, Bouchard).

CASE V. Boy, aged nine years, constipation, asthma, repeated attacks of coryza, furuncles (mixed form, Bouchard).

CASE VI. Male, aged forty years, constipation, chronic urticaria (cutaneous form, Bouchard).

CASE VII. Female, aged thirty-nine years, neurasthenia, anæmia (neurosal form, Bouchard).

CASE VIII. Male, aged twenty-two years, constipation, acne vulgaris (cutaneous form, Bouchard).

CASE IX. Boy, aged eleven years, constipation, extreme nervousness, migraine (neurosal form, Bouchard).

CASE X. Female, aged twenty-four years, constipation, chlorosis.

In all we took urine from twenty-four patients, thirteen of the former class and eleven of the latter; also urine from healthy persons, and with this urine one hundred and fifty-four animals were injected. All the experiments were conducted on the strictest principles of surgical asepsis. Details are unnecessary, except to state that all the instruments, vessels, and cotton plugs were carefully sterilized by heat before being used, and the fluid used for injection was always warmed. As it was impossible to obtain as many rabbits as were required, and, as Bouchard neatly puts it, "there are economical necessities before which it is necessary to bow," white mice were used in a large number of cases. That urine under proper conditions may become toxic to white mice was abundantly proven; but, in order to be positive in regard to this, in most of the experiments the ratio of 45 c.c. to 1 kilo of animal was increased to 100 c.c. to 1 kilo, or even more; but even with this enormous increase we arrived at the distinct conclusion that urine is less toxic to white mice than to rabbits. This was due more to the fact that more mice recovered after having been made ill than rabbits. The experiment, made to show the comparative toxicity of urine upon a mouse and a rabbit, does not, however, prove this.

EXPERIMENT XLVI. November 26, 1898, urine taken from a patient during labor, 33 c.cm., injected into a rabbit.

5.03 P.M.

5.13 P.M. Peculiar nodding motion of the head; throwing head to one side; rouses himself as though startled.

5.16 P.M. Head drawn backward, pupils dilated, but reacting to light; falls

on one side, jerking of all extremities; then jerking confined to muscles of neck; head thrown backward with convulsive motion; some clonic movements of head, ears, and forefeet.

5.17 P.M. Breathing stopped; heart still beating.

5.19 P.M. Lies on side, apparently dead; heart still beating.

5.19¾ P.M. Heart stopped.

EXPERIMENT XLII. Same urine, 2 c.c. injected into mouse at 9.10 P.M.

9.16 P.M. Drowsy, tending to fall to one side; breathing very rapid.

9.21 P.M. Violent trembling, lasting about one-half minute, then quiet, followed by trembling at regular intervals.

9.35 P.M. Wabbling gait; throws himself from side to side; trembling continues; rolling over, violent clonic convulsions, then tonic spasms with opisthotonos; seems to be struggling for breath; respiration very rapid; these cease and recur.

9.45 P.M. Death in clonic spasm.

The mice die in the same manner that the rabbits do, either quickly, in the manner just described, inside of an hour (thirty-five minutes, the longest time in our experiments), or in from twelve to twenty-four hours, the symptoms then being ushered in by drowsiness, lying down in the bottom of the jar, slowness of breathing, convulsions, and then death. The post-mortems have revealed nothing microscopically that could account for death; as far as bad results from the injection are concerned, we found lesions only in two instances (in the one—a mouse—a blood-clot in the omentum; in the other, a seropurulent, offensive fluid in the peritoneal cavity), except in cases in which the urine had been standing a comparatively great length of time, as will be referred to later.

The experiments began by investigating the urine passed by the patients mentioned above, in whom toxicity could be expected with reasonable certainty after reading the results of other investigators. It was shown here that in forty mice in only three the urine was toxic. Fresh urine injected immediately, boiled immediately and injected immediately; filtered urine never, but fresh urine when kept sealed to the utter exclusion of air, however, proved toxic in three mice. There seemed to be something in the urine, then, which had the power of rendering it toxic after sufficient time had been given to cause it to develop its activity. With this in view a large series of investigations was begun, with the results presented in the following table:

VARIOUS METHODS IN TESTS FOR UTERINE TOXICITY.

	Number of experiments.	*Result: deaths.*
Fresh urine injected immediately	Mice, 14	1
Filtered urine injected immediately, or after 24 hours	Mice, 21	None
Urine boiled immediately and used immediately .	Mice, 22	Mice, 2
" " " " .	Rabbits, 5	Rabbits, 2
	—27	14 per ct.
Urine boiled immediately and used after 24 hours .	Mice, 26	Mice, 10
" " " " .	Rabbits, 5	Rabbits, 2
	—31	39 per ct. +
Urine boiled with boric acid, allowed to stand 24 hours	Mice, 11	Mice, 2
" " " " " .	Rabbits, 3	Rabbits, 3
	—14	35 per ct. +
Urine mixed with boric acid, allowed to stand longer than 24 hours	Mice, 18	Mice, 5
" " " " " .	Rabbits, 5	Rabbits, 5
	—23	43 per ct.
Fresh urine allowed to stand for a variable length of time longer than 24 hours	Mice, 30	Mice, 20
		$66^2/_3$ per ct.

There are, then, one hundred and fifty-four experiments to draw conclusions from, arranged in seven series:

I. In the experiments made with the fresh urine the urine was passed into sterile vessels and injected into mice within a few minutes after it was passed. It will be seen that one mouse died. This is the mouse which had the lesion in the omentum, but died as all the mice died when the urine is toxic. It is difficult to say, precisely, how much the element of shock had to do with his death, especially in view of the fact that the same urine, after it had been boiled and kept for twenty-four hours, did not kill. The only other explanation that might be offered is the one that the operation was not done under strict asepsis.

II. For the purpose of filtration, urine was passed and then immediately placed in the filtering apparatus, either Kitasato or Chamberland. All the urine used by this method had first been tested as to its toxicity, and found non-toxic. It did not matter whether it was injected immediately or kept in sealed vessels for four days, it never produced death.

III. The urine that was boiled immediately and injected immediately—twenty-seven cases in all—had been tested in twelve cases for toxicity and been found non-toxic. In fifteen cases it had not been tested, so that no conclusion could be drawn as to the comparative effect of boiling. In the twelve cases it was not changed by boiling

in one way or another. In the fifteen cases it was impossible to make the experiment by injecting urine immediately drawn. The four deaths show that urine may be toxic when passed. It remains to be shown to what extent boiling reduces toxicity, if at all, on account of a possible effect upon it by ferments or other bodies, as well as by bacteria. The latter must be taken into especial consideration, because all of these specimens were taken from women immediately before, during, or immediately after labor.

IV. In urine that was boiled immediately and used after it had been kept the result was a peculiar one. The longer it was kept the more toxic it became. The following experiment was made to show this: 150 c.cm. was passed by a healthy individual; this was divided into eleven parts, all of which were boiled except one. This one was injected (1.5 c.cm.) into a mouse, and found non-toxic; the rest were boiled and put into Erlemeyer flasks. One of these was immediately injected into a mouse, and found non-toxic; the rest were injected twenty-four hours apart until all had been used. The result was death in all cases, notwithstanding the fact that the quantity of urine was reduced daily. At first the attempt was made to count the bacteria with an eye-piece micrometer, but this was very soon given up, on account of the enormous increase of bacteria. In these cases, after forty-eight hours, evidences of peritonitis was found in these mice, forming one of the exceptions to the rule stated before. The enormous mortality in this series of experiments, as compared with the general mortality (39 per cent.), is simply explained by the fact that all the other experiments were made in cold weather, from November to March, while this series was done during the very warm weather of spring (from 75° to 85° F., in the middle of the day). It seems, then, that boiling once is sufficient to kill bacteria, but not their spores; and, as in sterilized milk, as was shown by Flügge, the spores developed and finally produced the same effects as were primarily produced by the bacteria.

V. Some authors have recommended the addition of boric acid to prevent development of bacteria; for this reason the series was instituted. Here it was also shown that little influence was exerted, and that the longer the mixture was kept the greater the mortality. In a series published by one of us (Stewart, *loc. cit.*) the mortality was 100 per cent. In this series no account was taken of the time of taking

urine and its injection, although the table seems to show that urine kept with boric acid does not become toxic more rapidly than urine kept and used after being boiled; this, again, is on account of the difference in outside temperature, all of the experiments being made during cold weather.

VI. In regard to fresh urine which has been kept for longer than twenty-four hours, it need only be said that the largest mortality was arrived at by this method; and in some of the mice that lived longer than eighteen hours there were also present evidences of peritonitis.

As a result of these investigations we beg leave to present the following conclusions as to the method:

1. Fresh urine injected immediately can be safely used.
2. Filtered urine, immediately filtered and immediately injected, can be safely used.
3. Urine boiled and injected immediately should not be used unless error caused by possible changes within the body of the patient be first eliminated.
4. The addition of boric acid does not give reliable results.
5. Urine should never be used that has stood for twenty-four hours.
6. The method cannot be used for exact determinations of toxicity, in that a range of from 25 per cent. to 50 per cent. of error is found for individual cases.

The conclusion as to toxicity of urine can be only tentative as applied to all cases; but they are positive for the majority. If the table be examined, it will be seen that those two methods which exclude bacterial activity absolutely after the urine is passed are followed by comparatively no mortality; in fresh urine immediately used, only one death out of fourteen; in filtered urine, no deaths, even after the urine had been kept as long as four days; in urine with boric acid, used before the lapse of twenty-four hours, a mortality of 39 per cent., after twenty-four hours, a mortality of 43 per cent.; in boiled urine kept for longer than twenty-four hours, a mortality of 39 per cent; and in fresh urine kept for longer than twenty-four hours, a mortality of 66 per cent.

It would seem, then, that most of the toxicity of urine was due to the formation of substances the result of the action of bacteria upon some body or bodies in the urine. As a result of this investigation, we are not justified in stating that there is no other toxicity except

that due to bacterial activity, but we are justified in making this statement, that all those investigations that have been made in which this activity has been overlooked are to be regarded as inconclusive.

Finally, one of us wishes to make a scientific retraction of a statement made in a paper read before this Society. In connection with some investigations made upon chlorosis, one of us found a toxic body in the urine; this toxic body, in the light of the present investigations, was not the result of chlorosis but of a faulty method. In so far as this body has any effect upon the theory of the origin of chlorosis, this theory is hereby discarded.

THE IMMEDIATE AND REMOTE EFFECTS OF ATHLETICS UPON THE HEART AND CIRCULATION.

By ALFRED STENGEL, M.D.,
OF PHILADELPHIA.

During the past six years I have had frequent opportunities of examining athletes competing for positions and playing upon the various teams of the University of Pennsylvania, and have made studies, as far as was possible under the circumstances, to determine the effect of athletics upon the size and efficiency of the heart and the character of the circulation. It has not been possible for me to carry on elaborate investigations into the manner of production of the various phenomena which attend exercise, and I shall not enter upon any discussion on this aspect of the question now.

In outlining the heart of patients or athletes, I follow a method more or less like that used by Sansom. After carefully mapping out the heart's borders by percussion and auscultatory percussion, I mark these borders with a brush dipped in oil, and similarly mark the middle line of the sternum, indicating the suprasternal notch by a V-shaped figure at the top, the ribs (by broken lines), and nipple and position of the cardiac apex by a circular and a crossed figure respectively: A piece of soft tissue paper is then pressed over the chest, and in this way the outlines are secured in their exact size. The tracings which I present here are exact copies of such outlines upon heavier paper.[1]

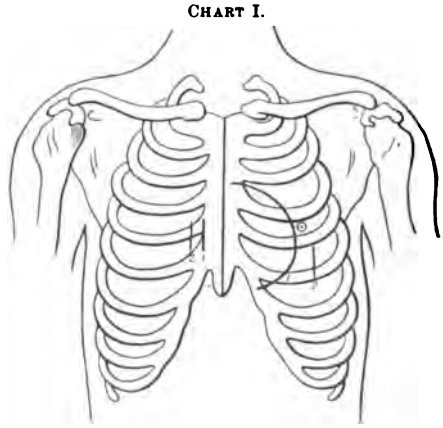
In watching the effect of training upon the heart, my attention was first directed to the ease of development of a systolic murmur over the heart. This occurred in the late summer of 1893, when I spent some

[1] In the reproductions accompanying this report accurate reductions, drawn to scale, have been used.

little time with the candidates for the football team during their preliminary training. The men who were candidates had, for the most part, been resting, and were, therefore, out of condition. I noticed that a systolic murmur over the body of the heart was not unusual, and in a special trial of nine of the candidates I found that three promptly developed a very evident murmur of the kind after a little exertion. During the subsequent fall term I tested the same men while in actual practice, and found that the murmur, before so readily produced, did not show itself. This led me to study the conditions of the heart immediately before and after exercise more carefully, the method employed being to map out the borders of the organ as already detailed just prior to some athletic sport, and again immediately after the exercise. I have prepared a number of such charts, of which a few may be taken as typical. The two first exhibited were prepared from young men rather new at athletics.

Chart I. was taken from a boy, aged nineteen years, who had not previously trained for any form of sport, and who was now engaged in one-half mile running. The chart exhibited represents the posi-

CHART I.



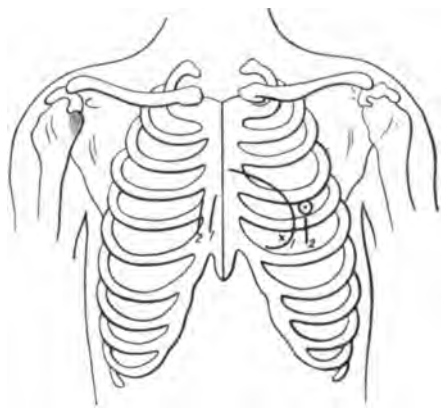
Illustrating position of the right and left borders of the heart before (1) and after (2) running one-half mile.

tion of the left and right border of the heart before and after a trial run of one-half mile. Before the race the sounds at the apex and over the body of the heart within the apex were normal, excepting for a certain deliberateness of the first sound. The pulmonary sound

was, perhaps, a little accentuated. There was a suspicion of murmurishness of the first sound toward the base of the heart. After the race the apex-beat was quick and circumscribed, and there was a distinct, diffuse thrill over the apex and in the epigastrium. Auscultation discovered a slight systolic puff, and the second pulmonary sound was distinctly accentuated. The murmur was localized in the region of the apex.

Chart II. was taken from the chest of a young man aged twenty-two years, a half-mile runner. Before the race, at the time of which this chart was prepared, the heart-sounds were found to be normal, though,

CHART II.



Borders of heart before (1) and after (2) one-half mile run.

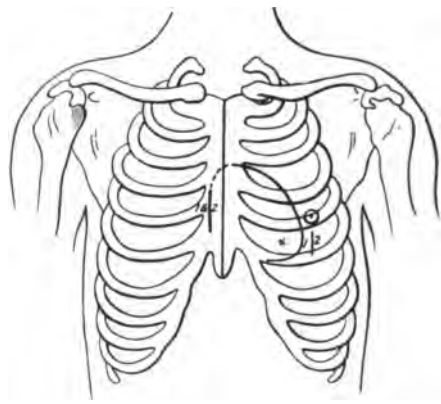
perhaps, a little quick and irritable. After the exercise a distinct systolic thrill was found at the apex. The first sound of the heart was murmurish, but the relative values of the first and second heart-sounds at the pulmonary area were retained. These two charts illustrate very strikingly the effect of exercise upon the heart in comparatively untrained young men.

As contrasts to these I select the next two which were prepared from trained athletes.

Chart III. was taken from a walker who had engaged in active athletics for a number of years, and who was unusually sturdy, walking in remarkable time a mile or more without any of the evidences of fatigue, so commonly observed after this sport. On the occasion on which this chart was prepared, Mr. F., a young man, aged about

twenty-three years, showed at the preliminary examination a strong and circumscribed apex-beat, with a long and very muscular first sound, but without a murmur. At the pulmonary area both sounds were distinct. There was a suggestion of a thrill on palpation over the apex. After walking three-quarters of a mile in very fast time, the apex-beat was found to be violent, and on palpation there was a

CHART III.



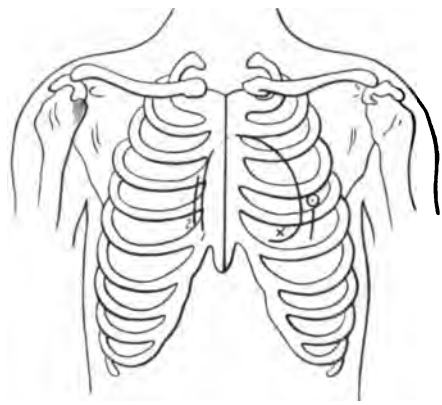
Borders of heart before (1) and after (2) three-quarter mile run.

rather more distinct thrill. The first sound was sharp and strong, but muscular, and there was a puffing systolic murmur heard over the pulmonary area, and accentuated by breathing, but the second sound was not particularly accentuated in the pulmonary area. The chart is mainly interesting in showing the right border of the heart exactly in the same position before and after exercise, though the entire organ seemed to be somewhat enlarged.

Chart IV. is that of a young man of remarkable physique, the holder of three world's records. The chart exhibited was taken after sprinting and hurdling. Prior to the exercise there was a systolic murmurishness at the apex, but no distinct murmur. The pulmonary second sound was about normal. The aortic second sound was a little accentuated. After the exercise there was a suggestion of a thrill in the region of the apex, and possibly also in the epigastrium. There was no murmur, but the pulmonary second sound was a little accentuated. In this case the right border of the heart was little affected by the exercise.

These charts are sufficient to illustrate the changes in the outline of heart as obtained by percussion and auscultatory percussion after exercise. I cannot now enter into a discussion of the causation of these changes, but should like to refer briefly to one or two points of interest.

CHART IV.



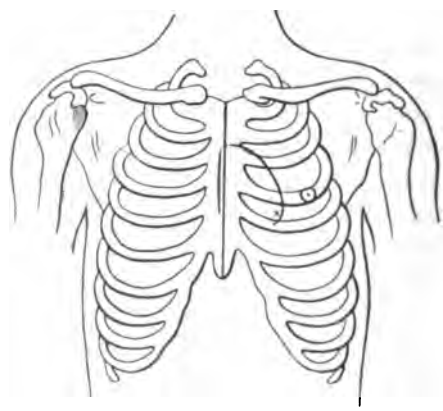
Borders of heart before (1) and after (2) sprinting and hurdling.

It has been demonstrated by physiological experiment that muscular exercise causes a fall in the blood-pressure in the peripheral vessels, and probably a dilatation of these vessels. Under these circumstances we should not expect an increase in the size of the heart, and increased intra-cardiac pressure as the result of strain. It does seem, however, that in the beginning of exercise there is a temporary increase in pressure at the centre. It has long seemed to me that the phenomenon known among athletes as "second wind" was to be explained by the recovery of the right ventricle after the preliminary overdistention incident to exertion. I had not seen this view expressed until within a few days, when my attention was called to the recent article by Dr. Allbutt, in his *System of Medicine*, vol. v. I quote from this article (p. 849): "The dilatation is, I think, concerned in 'second wind'; the healthy heart increases its output, the lungs expand, resistance falls, the right ventricle pulls itself together, and second wind is established. This process, trying enough to an unsound or defective heart, to young boys and to elderly men, is to the healthy heart of comparatively young adults perhaps never injurious." This expresses my view of the case exactly, a fact which is

all the more gratifying to me because Dr. Allbutt's views are based upon observations of under-graduates at Cambridge, as mine have been upon students in Philadelphia.

It seems to me not unlikely that the size of the right ventricle depends upon the degree of recovery of the right heart after the first distention. I cannot, however, agree entirely with Allbutt in the statement which follows immediately after what I have quoted: "I have many times seen under-graduates and others look ghastly at the end of a long spurt of exercise, but I never saw a sound young man the worse for a temporary stress of this kind; if, as in a few cases which I have seen again and again in growing youths, dilatation of the heart occurs, leading to cyanosis, panting, confusion, or vertigo, this oppression is generally sufficient of itself to stop the exercise in time." Of course, all of us who have had occasion to observe athletic sports of any kind have seen instances of the sort alluded to in the sentences just quoted, but I have seen a few cases in which recovery was not as prompt as is intimated, and in which, though a seemingly normal condition, was restored after a short interval, it seemed to me that some sort of permanent damage must have been done, though I could not demonstrate it.

CHART V.

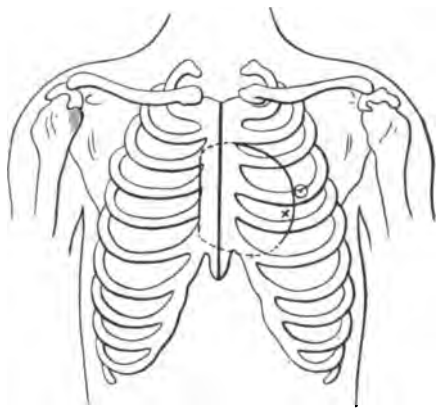


Football player and oarsman; outline of heart in 1894.

I may cite, for example, the case of a young man playing football, who was in superb physical condition, and was never known to be hurt or disabled in any way, and who, on the occasion of a trying

game, both physical and mental, toward the end of the game suddenly collapsed. I had repeatedly examined him prior to this time, and

CHART VI.



Same person; outline of heart in 1898.

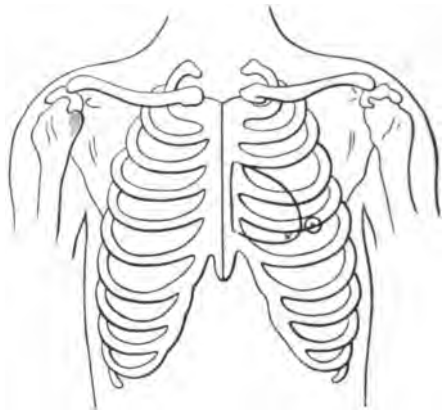
within a day or two had outlined his heart and other organs. I saw him immediately after his attack, and found him bleeding at the nose, more or less cyanosed, and with a weak fluttering pulse. On examination of his chest I discovered that both sides of the heart had become enlarged, the increase in size toward the left and right being fully three-quarters of an inch or an inch. The man was prostrated, and did not recover any sort of control of himself for some hours. He then grew rapidly better, and after a few days was seemingly quite well. He did not engage in football for ten days, but at the end of that time resumed practice and regular play without any apparent evil consequences.

A case of similar nature is the following:

W. R., aged nineteen years, weighed 122 pounds during the winter of 1897. During the spring and summer he rode a bicycle excessively, frequently riding twenty-five miles in the evening after his day's work. His weight declined to 109 pounds. In August he went to the seashore, and while bathing his strength was overcome by too much exertion at swimming, and he began to expectorate blood. The next day and during the days of the following week there were repeated hemorrhages of the same sort. The total loss of

blood was not very great, however. There was at the same time shortness of breath and cough on the very slightest exertion. The heart became intermittent and very tumbling in action, and both sides in-

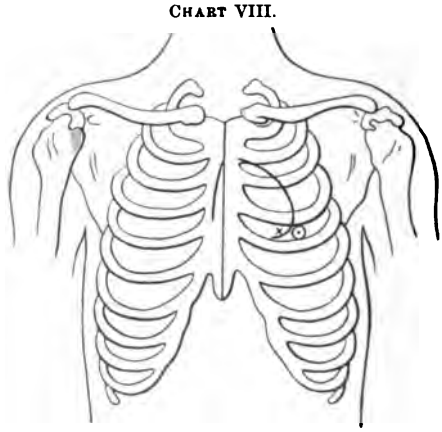
CHART VII.



Football player; outline of heart in 1893.

creased in size; the left border being in the nipple line, the right border beyond the right border of the sternum. There was no murmur even after exertion, when I examined him some time after the

CHART VIII.



Same person; outline of heart in 1896.

onset; the second pulmonary sound was a little accentuated. In this case, of course, the patient had not been in perfect health prior to his

overexertion, for he had been progressively overtaxing himself during the spring and summer.

Another instance of a similar character occurred in a patient, J. A. de F., a young man, aged twenty-four years. A year before he came under my observation he had taken a long bicycle ride, when he was not in a good physical condition, and the symptoms began immediately after. He had been working in an office and was not in a good condition when he undertook a four days' ride on a tandem bicycle; the minimum daily distance being fifty miles, and the maximum seventy miles. He was prostrated at the end of the four days. His heart became very irregular, and he was confined to bed for four months. At the present time his heart extends beyond the left mammary line and, on the right side, to the border of the sternum. There is a suggestion of a systolic thrill and murmur at the apex, but no positive signs. The second sound at the base of the heart is not accentuated.

These instances are sufficient to show that rather unfortunate results may occur from violent excessive exercise in young persons not in proper training, and even at times in those well trained. At the same time, the charts I have presented illustrate the fact that there is a decided difference in those who are carefully and those who are insufficiently trained. With Dr. Da Costa, who discussed this question many years ago in his Toner lectures, I should be most unwilling to see danger in athletics unless the proof were positive. There is, of course, a certain amount of danger in every sport, but the danger in athletics is certainly not very great. The necessity, however, of careful training, not only for the combats of the athletic field but for the general struggles of life, is demonstrated by my observations.

Alluding now to the question of the auscultatory sounds over the heart, I recall the fact that in numerous instances I have discovered a systolic murmur over the body of the heart at the pulmonary area and at the apex. It is by far most common to find this at the pulmonary area, and in young boys it seems almost habitual. This murmur is usually attended by a pulsation over the pulmonary area, and on careful percussion I have found that the oblique border of the heart was somewhat convexly curved toward the left. From these facts and other considerations I have become convinced that the cause of the murmur is to be found in a dilatation of the conus arteriosus. The murmurs at the apex may undoubtedly be due to mitral regur-

gitation, but I cannot convince myself that all of those found in this situation are of this nature. Some, I believe, are intra-ventricular; others, possibly cardio-pulmonary in origin.

With regard to the second point in the heading of my paper—viz., remote effects of athletics—I can speak only of the remote effects in the sense of the results following at intervals of a few months or years I believe that there is also a possibility of development of symptoms many years after cardiac strain, without any indications in the intervening time. We all recall the interesting publication of Dr. Morgan on the *University Oars*, being a study of the after-health of men who rowed in the University boats of Oxford and Cambridge between the years 1829 and 1869. I would also direct attention to the Toner lectures of Dr. Da Costa, delivered in 1874, in which he called attention to the possibility of strain as a result of baseball. In my own experience I have found a number of instances of distinct symptoms of cardiac disturbance in athletes who had devoted themselves rather steadily to various sports during their collegiate life. As cases in point, I shall briefly refer to the following notes:

C. S., aged twenty-five years, played football steadily at his preparatory school, at college, and during his university years, and baseball less regularly during the same time. After his graduation and his entrance upon active duties, he complained of a feeling of oppression in his chest, which he described as a sensation of distention, as if the heart was too large for the body. Sometimes there was palpitation and nearly always a consciousness of the heart in some form or other. His heart extends as far as the mammary line, and to the right border of the sternum, but there is no murmur or any sign of valvular trouble. He finds that the use of tobacco and alcohol, in which he has always indulged moderately, are prone to produce unpleasant over-action of his heart.

H. W., a football player, oarsman, and hurdler, steadily followed athletics during his college years. He now complains, after a few years of cessation of athletics, of symptoms similar to those just described. In particular he has noted a tumbling sensation in the heart beat from time to time, and he sometimes feels a sensation of oppression or dyspnœa.

C. G., a football and baseball player during six years, has complained, since his cessation from athletics, of vague oppression, fulness

in the chest, and some dyspnœa. He has, however, grown distinctly stouter in the two years during which he has relinquished exercise.

These cases will suffice to illustrate the kind of symptoms met with. I have seen many instances of this sort, and in seeking to explain their causation, have naturally been interested in the condition of the heart itself. The charts which I exhibit (Charts V., VI., VII., and VIII.) are selected to show the increase in the size of the heart resulting from several years' athletics. Others might be presented to illustrate the same point. It will be observed that in these cases the right and left ventricle increased decidedly in size during the three or four years that elapsed between the first and second examination. In each of the men from whom these charts were taken symptoms of the sort referred to were found.

Allbutt, in the article before alluded to, in mentioning the after-effects of athletics, suggests that the mean blood-pressure increases as a consequence of the withdrawal of the reducing influence of exercise. I have not been able to assure myself that the blood-pressure was actually raised, as I have found the sphygmomanometer an uncertain instrument, and I cannot bring myself to trust in the evidence afforded by direct palpation of the artery. I am, however, quite ready to believe that the blood-pressure is increased on account of the evident hypertrophy, if for no other reason. In athletes who have ceased to indulge in sports, and who have for some years suffered with symptoms of oppression, there seems to be a decline of the symptoms mentioned after some years and a return to more normal conditions. I am led to make this statement from the history obtained from individuals in middle life who had been athletes during their college years. My experience has not, however, been long enough to follow such cases from the beginning, and I hesitate to make assumptions in cases which I had not the opportunity of examining in the beginning. On the other hand, observations which I have had the opportunity to make in persons past middle life who had been very athletic in youth, have led me to believe that muscular disorders of the heart may arise in later years as remote consequences of overexertion in early manhood. I do not speak at length of these, because they are cases in which I have no means of knowing the conditions in the intervals between the beginning and the final trouble.

From the observations that I have been able to make, it seems

positive to me that overdistention of the heart is frequent in athletic contests, and may cause harm if the individual is in ill-health or badly trained; and, secondly, that hypertrophy and symptoms of overaction sometimes result from continued athletics. As practical conclusions, I would suggest rigid medical supervision of college athletics; and, secondly, that young men be encouraged to continue some form of exercise after discontinuance of regular athletics.

DISCUSSION.

DR. JACOBI: Were the X-rays employed for ascertaining the size of the heart?

DR. STENGEL: Not in any of these cases.

DR. MEIGS: Research carried on in the direction of that which has been undertaken by the author of the paper to which we have listened is likely to be fruitful. The subject of hypertrophy of the heart has been much studied, but the study has generally been of hypertrophy resulting from ordinary disease. With regard to the effects of exercise, and of contests, and overexertion in athletics upon the heart there is not much known. If clinical study of the effects of exertion is diligently pursued, it is most likely that at some time the opportunity will come to connect post-mortem results with clinical observations. I have long held the opinion that what is called compensating hypertrophy of the heart has been made to explain much with which it has, in truth, no connection. There is no doubt that a muscle which is exercised or subjected to resistance in its action will increase in size, but it will increase to a much greater extent in efficiency, and its capacity to increase in size is confined within narrow limits. All trainers know that but few men can be made great athletes. I do not believe that hypertrophy of the heart inevitably follows the leaking of a valve as a result of the action of the laws of hydronamics. I believe that the hypertrophy, when the enlargement is sufficient to be clinically recognizable, is a disease and is not conservative.

The doctrines that were generally accepted twenty years ago in regard to Bright's disease and the hypertrophy of the heart so commonly associated with it have fallen almost entirely into discredit. We used to be told that kidney disease caused increased resistance within the arteries, and this throws more work upon the heart, which in answer underwent hypertrophy and grew strong. Little is heard of this any more, and Bright's disease is less and less frequently used as a diagnostic term, for it is now recognized

that the rôle played by the kidney in chronic disease is not so overmastering as was supposed; but the kidney is only one of several organs, each one of which is of equal or nearly equal importance.

If hypertrophy is a process to compensate for the waste of energy caused by leaking of valves, why is it that many of the largest hearts that we see at post-mortem examinations are free from valve disease? All the hypertrophied hearts that I have examined with the microscope—and I have examined a great many—were composed of diseased muscular tissue. A number of times I have seen valve disease which had caused regurgitation, and yet there was no hypertrophy of the heart. If it is true that leakage does not always cause hypertrophy, and that the muscular tissue of hypertrophied hearts is always diseased, how can the conclusion be escaped that the doctrine of compensation by hypertrophy is fallacious?

Briefly, what I wish to express is this—it is my opinion that the common view of compensatory hypertrophy is probably theoretically correct, for it has a germ of truth as its foundation in that muscle does increase in size as well as in efficiency if subjected to increasing resistance, but as an explanation of enlargement of the heart I believe it is untenable. The large hearts that we are able to feel heaving within the chest during life, and which at autopsies we see to be of twice the natural size, are diseased and feeble. Hypertrophy of the heart is, I think, a condition parallel to hypertrophy of the liver and to hypertrophy of the kidneys, the increase in size is vicious, and was so almost from its origin, and it is a destructive process and is not compensatory.

Dr. Folsom: I think it is quite true that there are a certain number of ill-results brought on by unwise muscular training, but I think that where it is done wisely there cannot be quite so many as supposed; and even where there is distinct valvular disease of the heart from systematic muscular exertion, if not severe, the exercise would be of benefit. I remember a case whom Ziemssen saw with me in Munich many years ago, of a gentleman who had mitral insufficiency, but who has kept up vigorous exercise ever since then, and is now very well. From the cases I have seen I am inclined to think that a great many of the bad effects, if not the majority, come from one or two causes, either where a young man enters into athletics without a very good heart, as shown by persistent rapid pulse, or, more commonly still, from the want of systematic development of the muscles of the body. A good many of the young men who come to college and go into athletics are men with big frames and strong muscles, who have never been accustomed to severe muscular exercise, and go into athletics without realizing that it is easier to strengthen the muscles of the legs and arms than the muscles of the heart, and it takes more care to bring the heart up to the proper point than the rest of the muscles of the body. It seems to me if the young man was looked over pretty carefully first, and his development made with care, such cases as Dr. Stengel reports would be very much diminished.

DR. PUTNAM: I want to call attention to the fact that Dr. Prince many years ago wrote an excellent article on the prevalence of systolic murmurs, which afterward entirely disappeared, among candidates for the position of policemen, when coming up for examination. He proposed an ingenious theory, in which he attributed it to the nervousness of the men.

DR. DOCK: In a short experience with athletes, I have been impressed often with the importance of the pulmonary circulation in the production of the cardiac conditions mentioned. I have often noticed symptoms of acute emphysema, and in one case particularly, where the man training for the football team was very dyspnœic and the liver dulness extended down to the eighth rib on the right side. In many of these cases the men are not trained in expiration; either from ignorance or from local disease in the nose in some cases they expire very imperfectly. The man I referred to was incapacitated for work in this way. He himself realized he was not expiring properly and did not get his second wind, the acquisition of which seems to depend largely upon proper expiration.

It is not sufficiently borne in mind by many that athletes with apex murmurs may be capable of a large amount of hard work. I have seen that in the case of a celebrated half-back, who played a successful and hard game with my consent after he had been advised by other physicians not to play. I saw at the beginning of the late war a man who had been examined and rejected by the board of surgeons. I was told that if I could certify the man was capable of doing his work he would be admitted to the army by the higher powers. I had, therefore, to give a certificate which would get around the question of murmurs. The man was known to me personally as an athlete, and had an enlarged heart with apex systolic murmur. I put him through some tests, as the result of which I felt able to say conscientiously that he was fit for service. He went all through the service in Cuba and Porto Rico and has stood it, and better than the men who rejected him.

Such men are capable of a large amount of physical work, but, of course, I am well aware of the later dangers in such cases, and would not wish to lessen the interest paid them.

A STUDY OF A CASE OF FAMILY PERIODIC PARALYSIS.

By JOHN K. MITCHELL, M.D.,
OF PHILADELPHIA.

THE curious condition of periodic paralysis is one of the utmost rarity, and in this country but three cases have been seen, with a doubtful fourth, previous to the ones herein reported. I should omit from the consideration the cases of Rich, where the paralysis was directly due to a hereditary susceptibility to cold, and was distinctly spasmodic in character. Gibney's cases, supposed by him malarial in origin, certainly do not belong to this group either.

I do not propose to enter into the history of the previous study of this disorder, except incidentally. An admirable paper, by Dr. E. W. Taylor, in the *Journal of Nervous and Mental Disease* for September and October, 1898, contains a very complete bibliography of the previous work, with analyses of all the cases hitherto reported, and to this I am not able to add anything except my own cases.

All the cases observed have presented, with small variations, the same type—a paralysis of the voluntary muscles, usually total except for the head and face muscles, with loss of reflexes, with absence of electrical reaction, with no mental or sensory disturbance, and occurring periodically at somewhat regular intervals. Nearly all of the cases have instances in the parents or ancestors of the patient. In the family of my patient the first one known to have suffered from it was the maternal grandfather of the present victim, a Pennsylvanian by birth, a tinsmith by trade, who had in early life seizures like those from which my patient has suffered, but much less severe. A first cousin of this same grandfather had periodic attacks of paralysis quite as bad as any which have been described. His business kept him travelling much through the rough mountain districts of

Central Pennsylvania, and he used to say that he was often obliged to get off his horse and "have a paralysis." Both these persons, so far as known to their descendants, ceased to have the attacks in middle life.

The mother of the patient is one of six children. Of three elder sisters, none have ever had any spells of the palsy. An older brother had one attack, brought on by overexertion, but has never had another. A younger brother has suffered in the same way, but the attacks did not begin with him until he was a man grown, and have since occurred only at long intervals. A daughter of this brother, now between twelve and thirteen years of age, has periodic palsies of the same sort, and full details of these two cases follow my patient's history. None of the other cousins, except this one, has ever had the family affliction. The mother of the patient began to have periodic paralyses when fourteen years of age, probably at about the time when her menstruation appeared. Their approach was sometimes announced by a slight sense of helplessness, which would last for a whole day. Going to bed with this, she would wake in the morning with total muscular paralysis, usually lasting thirty-six hours, seldom longer, and never more than forty-eight. The paroxysms recurred at long and rather irregular intervals, often months apart, and after she reached adult life decreased in frequency with the advance of years, and ceased altogether at about the thirty-eighth year. She is now forty-four years of age and presents some interesting symptoms.

Mrs. E. J. is a well-looking woman, scarcely appearing as old as she is, calls herself perfectly well, menstruates regularly, and is active mentally and physically. She has a little difficulty in walking unless the ground is perfectly smooth; a very slight inequality makes her stumble, and if she stumbles she is very apt to fall. This is especially marked at night, when she cannot see where she is going, and has been noticed for some years. When sitting she gets up with some difficulty, rising as if her legs were weak, with a sort of wiggle, and aiding herself with the nearest object upon which she can lean. She thinks this is rather worse of late years, but she had not thought it bad enough to mention until her attention was called to it by questions. Her station is perfectly good, her pupillary reactions normal; the knee-jerk decidedly slow and small, a little better on the left than on the right; on the right there is no ankle-jerk, on the left

the ankle-jerk is present. There is muscle-jerk in both arms and in the left leg, but none in the right leg. Galvanic and faradic reactions are normal, and there is no alteration in sensibility. The state of things presents a somewhat mixed character, which, were it not for its very long duration, the absence of eye-symptoms and of pains, one might incline to think preataxic; but if it were of tabetic nature it would be symmetrical and not present entirely different qualities of knee-jerk upon the two sides, as it does, in these respects resembling rather the ataxic paraplegia of Gowers than true tabes. Her gait shows no abnormality whatever, but I incline to the belief that the repeated attacks of her earlier life have in some way definitely altered the lower segments of the spinal cord and impaired the control of the legs. There is no trouble with the functions of the bladder, rectum, or uterus.

The present patient, C. H. J., nineteen years of age, is a mechanic in a bicycle factory. But for the neurosis under consideration no hereditary disease is known on either side of his family. His mother's history has been given; his father is living and in excellent health; his younger brothers and sisters are well, although it may be said they have not yet reached the age at which the palsies usually appear. With the exception of the ordinary diseases of childhood, his own health has been perfect, his habits good, and his life an active and wholesome one until his present trouble began, in his thirteenth year.

The onset was sudden, without known cause. He awoke one morning and found that he could not move hand or foot; he was able to turn his head from side to side, but could not raise it from the pillow. There was no pain, no loss of sensation, no impairment of function of any kind. About two months after the first attack another occurred, and for three or four years they returned at intervals of about two months, with a duration generally of forty-eight hours, nearly always coming on during the night, so that the patient went to bed feeling no more than a trifling degree of enfeeblement in the legs, and awoke in the morning quite helpless. No possible cause can be assigned in his habits or mode of life. He cannot trace any single attack to excessive exercise, emotion, or indulgence of any description, and except that when they pass he finds himself a little sore and stiff for a few hours, he cannot see that he is otherwise than perfectly well in the intervals.

The intensity of the attack has remained about the same up to the

present, but for nearly a year past the frequency of occurrence has become rather greater, and for six months before he was first seen, in October, 1898, the paralyses had recurred with remarkable regularity upon Wednesday of every week.

It is well to say at once that nothing about the patient between or during the attacks suggests the slightest possibility of a hysterical element. He is a normal, healthy boy, well developed, in admirable physical condition, and much disgusted with the enforced idleness of this disablement. Many attacks have been seen in the hospital, and the various seizures differ only in the degree of immobility produced. One may be described in detail and stand for a type. Sometimes for a few hours in the afternoon or evening the patient notices slight weakness in the lower limbs, and if examined at this time at least one decided symptom is present—a lessening of the knee-jerk. This happened to be the case when I showed him one evening at the Philadelphia Neurological Society, when he said, after coming into the room: "I am just beginning to feel an attack coming on," and upon examination the knee-jerks were found to be capricious, diminished, and easily exhausted. This prodromal period is not always present. He may go to bed perfectly well and awake in the morning wholly paralyzed from the neck down. I say "from the neck down," but the neck to a certain extent shares in the difficulty. He can, when lying still, turn the head from side to side, but he cannot raise it from the pillow, and if placed in an erect position the head falls forward on the chest, or backward almost between the shoulders without the possibility of any control on the patient's part.

Breathing in the attacks is somewhat shallow, and appears almost altogether diaphragmatic in character. If he is requested to cough he is unable to, or even to take a normally full inspiration. If the nares are irritated he cannot sneeze, though he feels the annoyance and has a desire to do so.

He does not have much appetite, and says he perceives slight difficulty in swallowing, but this is not evident to the observer. While the paralysis lasts he usually passes water only once or twice in the twenty-four hours and has no fecal movement. There is no disturbance of the mind; speech is not affected, and he has no pain except the discomfort of lying absolutely in one position, which somewhat annoys him. So far for his own statement of his feelings and symptoms.

PHYSICAL EXAMINATION DURING AN ATTACK. The patient is notably paler in the attack than during healthy intervals. His lips are less well colored; his tongue is somewhat coated and his breath has a heavy smell, but there is no change of expression, and certainly no mental impairment. He answers readily to all questions and takes an interest in the examination of his symptoms.

Upon study of the chest the breath-sounds are found to show slight general lessening, due, probably, to imperfect dilatation of the chest. On being asked to take a long breath, he makes an effort to do it, but has little control of the accessory muscles, and moves the cage of the ribs but slightly. The heart's action and pulse are decidedly changed from normal. The apex-beat is below the fifth rib, rather indistinct, two and a quarter inches from the mid-sternal line. The heart's action varies much in different attacks; it is sometimes a little irregular in time, though no distinct intermittency has been observed at any time. The heart conditions, however, were not always the same during the attacks. Examined several times during October and November in attacks the heart presented usually a split second sound, very distinct in the pulmonary area, a systolic murmur well heard upon full expiration and limited to the same area, transmitted somewhat up and down the left side of the sternum, strong and decided, but not loud or harsh.

In the latter part of November, examining him one day with Dr. Morris J. Lewis, we both agreed that there was a soft, low systolic murmur, best heard at full expiration at the second right interspace and very faintly upon the left side. This was a condition which was never found again. Three days later, during an interval, the split second sound was heard at the second interspace, diminishing toward the apex, with a murmur much harsher than before, and of greater intensity. The most careful examination with stethoscope and phonendoscope fails to reveal any increase in the area covered by the heart dulness. The pulse is somewhat weak and small, from 80 to 90 during an attack; sometimes, with about the same speed, its tension is increased and its character distinctly dicrotic, as shown in sphygmographic tracings made repeatedly during the attacks.

The heart examinations were made over and over again. I made not less than a hundred careful examinations of the heart in the attacks, and as he was an object of interest to the other members of the

hospital staff, the examinations were made many times over by them, and the general opinion confirmed the above statements, which indicate rather a relaxed condition of the heart muscle, as well as of the whole arterial system, than an acute cardiac dilatation. In this belief I am supported by the high authority of Professor J. M. Da Costa, who studied the heart during an attack.

The reflexes in the more severe paroxysms are totally lost except the reaction of the pupil. No contraction can be observed in the pectoral muscles on striking them; the abdominal recti do not contract to ordinary stimuli, the cremasteric reflex is abolished, there are no knee-jerks, and although the patient resents the attempt to secure the plantar reflex by irritation of the sole of the foot, no muscular contraction takes place. Sensation is perfect. The electrical examination was many times repeated during the attacks and in the intervals. In the typical attack there was practically total abolition of reaction to any form of electrical stimulation.

In milder attacks some variations upon these general symptoms were noted. Muscle-jerks were sometimes present, the knee-jerks were occasionally found present by reinforcement, the cremasteric reflex was at times not altogether absent, though usually weakened. In the same way the degree of muscular enfeeblement varied a little. In the early part of even severe attacks, during the morning hours, the patient would be able to move his hands, perhaps his forearms, or even his toes. As the day went on the paralysis would become deeper and all movement would be abolished. Return of normal conditions followed much the same order that characterized the onset. The knee-jerks improved a little, other reflexes reappeared, slight contractility in the muscles was discoverable, and in the course of an hour or so from the beginning of betterment the patient was almost perfectly well. Several times periods of apparent partial recovery were followed by relapses into total paralysis. Usually progress was steady and rapid, and several times we have seen a man who at six o'clock was, so far as power to move or to respond to electrical stimulation could tell, as dead as a twelve-hours' corpse, able to walk about the ward at seven o'clock with all his muscular power, his reactions and reflexes, in normal condition.

Once at least, in the course of the several months the patient was under observation, he seemed to have a kind of abortive attack, in

which during some days he felt dull and had the same sense of lack of complete muscular power which usually precedes a paroxysm. At the same time his color was poor and his appetite not so good as usual. Knee-jerks during the whole of this period were found to be occasionally absent, though reinforcible, and at other times capriciously present, but always diminished. It should be added that this was during a time when he was taking bromide in moderate doses. One important fact developed somewhat late in the case, or at least had not been previously observed. Upon my remarking that I should give him injections of Brown-Séquard's elixir, and that it might have an effect in stimulating the sexual functions, he laughed, and begged not to have it, because he said there was sufficient stimulation in the attacks already, and that very often he suffered with a partial or complete erection during the period of paralysis.

[Copy of letter from the patient's maternal uncle, Mr. C. H. W., dated January 29, 1899.]

DEAR SIR: I am perfectly willing to give you all the information in my power, but hardly know where to begin. I have been subject to the attacks you refer to from the time I was twelve years old, but have never been completely prostrated since my marriage, sixteen years ago.

The disease (or spells as we called them) would sometimes come on me during the night, and, while feeling all right at bedtime, would be perfectly helpless on waking in the morning. At other times they would come on me gradually, and I could feel myself slowly losing control of my limbs, and finally became helpless; sometimes I could, by keeping in motion, keep from total collapse. I suffered no pain of any description, unless my limbs were cramped, but was perfectly helpless, could move neither hand nor foot, but seemed to have complete control of my talking apparatus, and with the exception of being helpless, I usually felt exceptionally well. My sense of feeling was normal, but the sense of motion completely gone. I noticed that the attacks were more frequent in damp weather; also, that they were sometimes brought on by unusual exertion.

My daughter has suffered from the same disease, but has been completely prostrated only a few times, and as it happened at a time when I was away from home, I will hand your letter to our family physician, Dr. H. L. McIlhenny.

[Copy of letter received from Dr. H. L. McIlhenny, Norwich, Kansas, March 10, 1899.]

MY DEAR DOCTOR: In reply to your letter of February 2d, will say that I am personally acquainted with Mr. W. and family, to whom you refer in your letter.

Referring to the peculiar family affliction, I have to say that I have seen Mr. W. a number of times suffering with these mysterious attacks—though he has suffered but few in the last few years. The condition is surely a most singular one, never having seen any cases like his or his daughter's, and have never seen any authority covering these cases.

Mr. W., I understand, has given you the details of his case, which are evidently very similar to the attacks with which J. suffers. As to Mr. W.'s daughter, who is now about fifteen years of age, I have seen her in this peculiar condition but once, about one year ago, although she has had two or three attacks since, but they were rather light.

At the time I saw her she had gone to bed in the evening as well as usual, and on waking in the morning she found herself completely helpless—paralyzed. I was called and found her in this paralyzed condition, could not move hand or foot. In all respects the attack was similar to those from which her father suffers, except that she suffered quite severe pains in back and head. All reflexes seemed weakened or absent. She remained in this condition ten or twelve hours, when she began to get better, and by the next day she could help herself and began to sit up. In three or four days she was as well as usual. There does not seem to be any regularity in her attacks, nor do I think that menstruation has any relation to the attacks. I hardly think mental emotion or physical exertion are exciting causes. This young lady has been away from home several months, attending school, and I have not heard of her having an attack recently. I forgot to say that in this case (Mr. W.'s daughter) I did not make a *careful* examination of the heart, only to note that the heart seemed all right.

The electrical examinations are of great interest, and have been often and carefully made by Dr. J. H. W. Rhein, electrician to the Infirmary for Nervous Diseases.

In the first examination during an attack it was impossible to get any reaction either with faradic or galvanic currents in most of the muscles with the largest amount of currents bearable. With from 30 to 40 milliampères slight response could be obtained in the anterior thigh muscles. It was impossible to complete the examination on account of the pain caused. In examining a large pad was always placed over the sacral region and a small interrupting electrode over the motor points of the muscle tested. The K. CL. C. contracture was always greater than the AN. CL. C. contracture.

On the second day of the same attack it was possible to get contracture here and there; for instance, the anterior tibial responded with 20 milliampères, the posterior with 18 milliampères, the sciatic nerves with 20 milliampères, and the biceps of the leg with 30 milli-

ampères. No contraction of the rectus femoris could be obtained with less than 30 milliampères. It was necessary to discontinue the examination, as the strong currents made the boy feel faint, and decidedly affected his heart.

In a second attack there was no faradic reaction whatever in most of the muscles. In the erector spinæ muscles there was fair contraction with the greatest amount of current that could be applied. The sternocleidomastoid responded slightly with largest amount of faradic current. This was true also of the other cervical muscles. With the galvanic current no response could be elicited in the cervical muscles with 20 milliampères. It was thought unwise to use larger quantities of this current in the neck region.

Examination in a third attack showed that the anterior tibial muscle responded with 20 milliampères on both sides, the posterior tibial with 12 milliampères on the right side and with 40 milliampères on the left, the erector spinæ with 20 milliampères, the abdominal muscles with 16 milliampères, the biceps, triceps, extensors, flexors, and deltoid responded with currents varying from 30 to 40 milliampères.

In the fourth examination, during a mild attack, the following conditions were found: 5

	Right.		Left.	
No contracture with	15	Anterior tibial,	15	No contracture with
	10	Posterior tibial,	8	
	10	Rectus,	18	
	15	Biceps,	15	
	20	Gluteus,	20	
	20	Erector spinæ,	20	
	41½	Flexors,	7	
	6	Extensors,	15	
	10	Triceps,	10	
	10	Biceps,	8	
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Biceps and anterior muscles responded very slightly to the greatest amount of current obtainable in a faradic battery, while the rectus and posterior tibial muscles responded fairly well on the left side. The posterior tibial and rectus on the right side reacted better than the biceps and the anterior group on the right side. The flexors of the arms contracted much more readily than the extensors, the biceps more readily than the triceps; the deltoids respond fairly well, the pectorals much more readily, the abdominal muscles only slightly; the infraspinatus responded fairly on both sides. No movement was obtainable in the supraspinatus on either side. The rhomboid muscles contracted quite well.

Median nerve transmission was 15 milliampères right and left. In order to lessen skin resistance as a factor, examination was also made with the limb immersed in water, but this did not seem to diminish the amount of resistance offered by the muscles to the faradic current.

During a profound attack, in which it required from 20 to 30 milliampères, CA. CL. C. being greater than AN. CL. C., to develop contraction by the usual method, when a large electrode was placed upon the sacral region and a gold needle inserted deep into the body of a muscle, it was found that fair contracture could be induced with 8 milliampères, CA. CL. C. greater than the AN. CL. C., interrupting current at the needle insertion into the muscle. On repeating this experiment upon a healthy person it was found that less than half this amount of current was required to evoke contraction in his muscles.

There has never been at any time any suggestion of reversal of the poles; CA. CL. C. has always been greater than AN. CL. C. in these examinations.

When the nerves were tested the same lowered irritability was observed—that is to say, if it took 20 milliampères to induce contraction in a group of muscles no less was required to bring about contraction when the nerve was stimulated.

Upon examining the patient during the interval and a few hours after the paralysis had disappeared, it was found that the muscles responded normally to faradic and galvanic currents, and that nerve transmission was in no way interfered with. This was repeatedly confirmed.

All these are elaborately detailed, because of the interest which attaches to the very absence of all possibility of stimulation, but may

be summed up by saying that during the attack, if it approached at all to completeness of loss of power, no electrical reaction was present to any current which it was possible to use upon a living human muscle, and even when the skin was pierced and electricity applied directly to the muscle a current very much greater than that which would move a muscle in normal condition was required to produce contraction.

The examination of the urine has been most painstakingly made for me by Dr. A. E. Taylor, at the Pepper Clinical Laboratory of the University of Pennsylvania, and his report is as follows:

Urine of Period of Attack, 935 *c.c.*

Total nitrogen, 13.749 g.	Total phosphates, 1.414 g. P_2O_5.
Urea, 24.510 g.	Alkaline phosphates, 0.574 g. P_2O_5.
Urea-nitrogen = 83 + per cent. of total nitrogen.	Earthy phosphates, 0.840 g. P_2O_5.
Uric acid, 0.526 g.	Total sulphates, 1.356 g. SO_3.
Xanthin bases, 0.283 g.	Preformed sulphates, 0.140 g. SO_3.
	Ethereal sulphates, 0.216 g. SO_3.

Urine of Interval, 1610 *c.c.*

Total nitrogen, 9.397 g.	Total phosphates, 1.306 g. P_2O_5.
Urea, 18.490 g.	Alkaline phosphates, 0.494, g. P_2O_5.
Urea nitrogen = 82 + per cent. of total nitrogen.	Earthy phosphates, 0.812 g. P_2O_5.
Uric acid, 0.194 g.	Total sulphates, 0.695 g. SO_3
Xanthin bases, 0.142 g.	Preformed sulphates, 0.546 g. SO_3.
	Ethereal sulphates, 0.139 g. SO_3.

Urine of Period just following an Attack, 1725 *c.c.*

Total nitrogen, 16.332 g.	Total phosphates, 3.084 g. P_2O_5.
Urea, 31.111 g.	Alkaline phosphates, 1.999 g. P_2O_5.
Urea-nitrogen = 88 + per cent. of total nitrogen.	Earthy phosphates, 1.085 g. P_2O_5.
Uric acid, 0.297 g.	Total sulphates, 2.174 g. SO_3.
Xanthin bases, 0.090 g.	Preformed sulphates, 1.975 g. SO_3.
	Ethereal sulphates, 0.199 g. SO_3.

Urine of Period of Attack, 1550 *c.c.*

Total nitrogen, 7.247 g.	Alkaline phosphates, 1.163 g. P_2O_5.
Urea, determination spoiled.	Earthy phosphates, 0.620 g. P_2O_5.
Uric acid, 0.103 g.	Total sulphates, 0.652 g. SO_3.
Xanthin bases, 0.0214 g.	Preformed sulphates, 0.561 g. SO_3.
Total phosphates, 1.783 g. P_2O_5	Ethereal sulphates, 0.089 g. SO_3.

Each set of analyses comprises the figures for the urine of twenty-four hours. The first two sets were done in the period when the

patient was upon milk diet; the last two were done while the patient was upon a mixed diet.

The total nitrogen and the urea, as well as the ratio between the urea-nitrogen and the total nitrogen, were within normal limits, in consideration of the diet.

The quantities of uric acid were, with the exception of the first analysis, notably low. There was, however, no constant relation; the highest and lowest figures were gotten for the urine voided during attacks, while the figures for urine voided between the attacks lie between them. Such fluctuations may, however, be seen in the urine of healthy people.

The xanthin bases were in three of the four examinations excessive. In the urine of the last attack the quantity was entirely normal. Such a quantity as 0.090 g. may often be seen in various diseased states, but figures such as 0.283 g. are rarely seen outside of leukæmia. Whether the quantities of uric acid were small because the xanthin bases were eliminated as formed and not oxidized to uric acid cannot be shown.

The elimination of total phosphates was within the normal limits. In the first two analyses a reversion of the normal ratio between the alkaline and the earthy phosphates was determined; in the last two analyses the ratios were normal. This reversion of the ratio between the alkaline and earthy phosphates is considered by Gilles de la Tourette to be diagnostic of hysteria. It is, however, found in very few cases of hysteria in this country.

The total sulphates were in all analyses within the normal limits. The normal figures for the preformed sulphates indicate that the proteid metabolism was normal. The quantities of ethereal sulphates were low. The diet and the colonic lavage obviously have tended to limit the formation of the ethereal sulphates, and the figures certainly indicate that there was no excess of proteid decomposition in the alimentary tract.

The urine of twenty-six days, including three attacks, was carefully tested for ptomaïnes, alkaloids, and alkaloidal substances by the Brieger and the Baumann-Udransky methods. No trace of such substances could be detected. These tests do not reveal bacterial toxines in the true sense of the term, and a rôle on their part in the case cannot be excluded.

The urotoxic coefficient (determined according to the Bouchard method, except that the injections were done under slight ether narcosis into the jugular vein) was below 0.536 for the urine voided during the attack and below 0.557 for the urine voided between the attacks —I say below, because in each case the injection was stopped at a point when the rabbits were apparently dying, but in each instance the animal recovered. In consideration of the diet, of the fact that the man was in bed, and that the injections were made into the jugular vein, the urotoxic coefficients were normal. The close approximation of the coefficients in and after the attack is striking, and speaks against regarding the seizures as corresponding to variations in the urinary toxicity As a matter of fact, the Bouchard procedure is crude, and under all circumstances furnishes results of doubtful value. I do not believe the negative results in these injections can be taken as a serious consideration against the view that the seizures may have a toxic cause.

Chemical and bacteriological studies of the feces during and after several attacks gave negative results, which it is not necessary to detail.

Studies of the blood under the microscope revealed little or no changes. No malarial protozoa could be found in any form. With stained slides the relative proportions and staining reactions of the different elements were found unaltered. Counts of the red and white corpuscles gave normal results, and the percentage of hæmoglobin was always high, never having been found below 90.

I asked my friend, Dr. Alfred Stengel, to repeat these examinations, which were made by myself and by my hospital assistants, that I might have the advantage of an authoritative opinion, and to undertake some experiments to determine the toxicity of the blood-serum. In bleeding the patient to secure the necessary amount of blood for these experiments a remarkable difficulty was experienced. When the median cephalic vein was opened during an attack the flow of blood was so slow and so small that we could hardly secure the six ounces we wanted. Thinking the opening in the vessel had not been large enough, on another occasion we cut the vein right across, but with scarcely a better result. The patient's heart-action at the time was, as usual in the paroxysms, rather rapid and feeble, with lowered pulse-tension, and on the occasion when we abstracted the full six ounces he felt decidedly light-headed before the bleeding ceased.

Dr. Stengel's report is as follows:

"*November* 22, 1898. 1. Five c.c. of serum from blood drawn during an attack injected into rabbit weighing 1550 grammes at 4.30 P.M. Was well at 6 P.M.; died during the night. Post-mortem showed abundant hemorrhages at base of right lung; less at left base. No other changes of a definite sort.

"23*d*. 2. Injected with same serum, 2¼ c.c., rabbit No. 2. One hour after: Red corpuscles, 5,012,000; white, 9800. Twelve hours later: 6,000,000 red cells and 11,550 white.

"*April* 28, 1899. 3. Injected 5 c.c. of serum into rabbit weighing 2250 grammes. Rabbit alive after forty-eight hours.

"4. Injected 9 c.c. into rabbit weighing 2150 grammes. Died in thirty-six hours."

These may be considered as wholly negative results, certainly not indicating any unusual degree of toxicity in the blood.

The consistency of the manifestations in the attacks is remarkable. In twenty-five attacks observed the only difference was in the degree to which power was lost, the more or less total disappearance of reflexes, and the varying occurrence of certain changes in heart-action and pulse-tension.

Almost all of the eighteen or twenty cases observed by various writers in Europe and in this country have presented symptoms very closely alike. In almost all paralysis has been periodic in its occurrence; generally there have been instances among relatives of the sufferer; in none have any sensory changes been found, and in those in which electrical study has been made electrical changes which greatly resemble the ones here described have been present, and in the intervals of the attack the patients almost invariably give the same history of complete and perfect strength and soundness.

I say that in all the cases there have been practically no sensory changes. One described by Fischl had distinct impairment of sensibility. This case is in other ways a rather doubtful one, and might perhaps be excluded from the list.

Oppenheim and Hirsch both describe temporary slight increase of cardiac area, and both have observed murmurs upon which the diagnosis of probable mitral insufficiency was founded, a condition which lasted only during the paralysis, and disappeared rapidly with the return of power.

In one of Goldflam's cases irregularity was observed and a faint systolic basic murmur. In mine, as has already been indicated, there was a murmur, limited to the left edge of the sternum, and best heard at the pulmonary area. This condition has varied very much in the different attacks, but this is the one which is most common. As a rule, J.'s heart is faster in the attacks than out of them, in spite of the complete absence of muscular movement. A slight accentuation of the second sound with a tendency to splitting is present even in the intervals.

The examinations of the blood, feces, and urine have been made in most careful and detailed manner, and the results herewith call for but one comment—namely, that most minute study has revealed no fact of importance in any of them, and in the two or three cases in which these points have been thoroughly gone into, almost equally little has been learned from the examinations.

As to treatment, it may be readily supposed that this has been experimental. For several weeks during the early observations J. was not given any medicine, but led a perfectly regular and wholesome if somewhat inactive life. This was thought advisable, in view of the fact that several cases have described their paralyses as brought on by overexertion. No such cause could be assigned in the present instance, as for some weeks he lived in the hospital ward and moved about the building freely, taking the ordinary liberal house-diet and being under close observation. The first theory which suggested itself, as it has to other observers, was that the trouble had an autotoxic origin. In order that there should be no retention of feces in the intestinal canal to favor this, the colon was carefully washed out every second day. During this period attacks occurred exactly as regularly as they had before he came to the hospital. He was then put to bed and kept upon milk-diet; the colon washing was continued and various intestinal antiseptics were used. The attacks recurred with about the same interval as before. He lost a little weight upon this treatment, during which also massage was used, for the sake of keeping up his circulation and of anticipating the impairment of digestion from inactivity. It was during this time that the first studies of the urine were made by Dr. Taylor, and his examination showed one of the effects of colon lavage in the absence or lessening of the ethereal sulphates. Finding the paroxysms recurring as be-

fore, he was allowed to get up and move about a little, but the amount of milk was increased, and soon after he was returned to house-diet. At this time the later examinations of the urine were made. No evidence having been secured from the urinary and fecal examinations of any toxic condition, intestinal antiseptics were stopped and an attempt was made by the use of full doses of strychnine to stimulate the spinal cord, upon the secondary assumption that this might be the source of the disturbance. Full doses of strychnine were given and rapidly increased, and if any change took place in the patient it was that the attacks appeared at rather shorter intervals than before. Strychnine had a very decided effect upon him, and it was not long before it had to be stopped. For a time he was left without any treatment, with orders to the hospital people to occupy him as much as possible and to let him go out every day for a walk. No decided difference in the frequency of paroxysms appeared under this regime, and for a time under no treatment at all the attacks, without evident cause, grew somewhat more frequent and recurred several times with only three or four days' intermission. Bromide was then given, and the first week of its administration in doses of twenty grains three times a day there was no "spell," although just previously the intervals between attacks had been, at the utmost, four days. He was rather long in the next seizure, which was a very complete one, and when he recovered from it he had a week during which the knee-jerks were irregular—sometimes absent, sometimes slightly present—and in this whole period the patient felt dull and not so strong as usual upon his feet.

Little as we have discovered of any unusual condition of the blood, feces, or urine in this cases, it seems to me impossible to attribute the attacks to any other than a toxic cause, even in face of the negative results of the chemical studies. The analogy is sufficiently striking to some other autotoxic, or partially autotoxic disorders, in spite of the want of direct findings to support this view, and in spite of the fact that some aspects of the case are against it.

In migraine, for example, we have an instance of a disease in which family tendency is strongly evinced, which usually begins about the age of puberty and lessens or disappears in middle life, which occurs paroxysmally and often at fairly regular intervals. The manifestations of migraine are largely cerebral, and those of the disorder we

are considering appear in the spinal centres and peripheral nerves and muscles.

As to other possibilities, it has been variously suggested that, as in the cases described by Higier, and lately in Philadelphia by Dr. J. W. McConnell, the attacks are the paralytic equivalents of epileptic fits. But in the instances where paralytic seizures have replaced epileptic paroxysms no alteration in electrical reactions has been found, so far as I know, nor any loss of reflex and direct muscular irritability, nor are heart-murmurs produced. The perfectly clear mind of the patient throughout the attack is also against this supposition, and so is the long duration of the palsy.

The suggestion of hysteria is scarcely necessary to discuss. The altered electric reactions, the absence of reflexes, and the perfectly well-balanced, wholesome moral tone of the patient, at once negative this.

A poison, or more than one poison, formed at intervals or constantly formed and gradually accumulating, and acting severally upon the heart and vessels, the spinal centres, as shown by the sexual excitement, and upon peripheral nerves and muscles, is the most warrantable conclusion. It is difficult to imagine one toxic material which should have all these effects; but certainly no one could study this boy's state and not have poisoning suggested to his mind. The heavy breath, the coated tongue, the comparative suppression of urine during the attack, with an unusual flow after, all carry out the analogy to migraine. If one poison might act upon both spinal centres and peripheral nerves and muscles, it is, perhaps, not too fanciful to account for the heart conditions by supposing that the resulting total flaccid palsy may extend to the muscles of the arterial system, and that this relaxation allows of so much dilatation of the great vessels as to favor the production of a murmur.

Some additional testimony to a special action of the poison upon the cord may be drawn from the examination of the patient's mother, in whom there was distinct, if slight, enfeeblement of function in the lower spine.

On the whole, upon due consideration of all the cases that can possibly be included in periodic family paralysis, it appears to be a warrantable conclusion that two poisons are formed, one of which predominates in some cases, another in other cases; according to the

predominance of one or the other, the effect is greater upon the peripheral nerves and muscles or upon the spinal centres. The disease is remarkable in this that it is clinically a most distinct entity, that all observers agree in their statements of the vast majority of symptoms, and that up to the present time the causation and pathology of the affection remain in absolute darkness.

DISCUSSION.

DR. PUTNAM: I have observed one case almost identical with Dr. Mitchell's, but I have not seen the patient during the attacks, and so have not made the crucial test with the electrical reactions. The attacks come on about the same way, however, sometimes with previous enfeeblement, and the paralysis is absolute, involving everything except the lips and eyelide. It lasts from one to three days, but in light attacks perhaps only for a few hours. The same peculiarity is observable here, too, that the attacks occur on a particular day—almost always on Sunday. That led me to think of some peculiar hysterical element, and I am glad to have that feeling removed by the statement of Dr. Mitchell concerning his patient. My patient takes no food during the attacks, as he has the feeling that it makes him worse. With him, also, the attacks come on occasionally, perhaps, after overexertion, but at the same time he is a powerful young man of twenty-four years, an expert cyclist, with large, strong muscles.

Dr. Taylor, my colleague, was, I believe, the first one to describe a case in this country, which occurred in the family of a student now in the medical school. In the family of my patient no other case has occurred, but I suppose there must be a beginning somewhere.

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